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Surgical Shock

and the

Shockless Operation Through Anoci-Association

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Second Edition of "Anoci-Association"
Thoroughly Revised and Rewritten

Edited by

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PREFACE TO THE SECOND EDITION

ACCUMULATING experience in the civilian clinic and in field and base hospitals in France has added so much corroborative evidence of the soundness of the fundamental principles of anoci-association and of its practical application, that we have ventured to rewrite and augment our former volume.

As in the first edition, our purpose is to present as concisely as possible the principles upon which the doctrine of anoci-association is based and their practical application. To this end we have omitted any discussion of the various theories of shock.

G. W. CRILE.
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CLEVELAND, OHIO.

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INTRODUCTION

THE EVOLUTION OF THE THEORY OF SHOCK AND THE SHOCKLESS OPERATION

In 1893 we began an experimental investigation of the comparative effects on the blood-pressure and respiration of traumatism of different kinds and of varying degrees of intensity inflicted upon various parts and organs of the body. These researches were published in detail in 1897 in a monograph.[1] In this research we found that shock is most readily caused by trauma of the parts most richly supplied with sensory nerves; that the more intense the trauma, the more rapid the production of shock; that hemorrhage and asphyxia predispose to shock. These observations led us to the conclusion that shock is a state of exhaustion; and since, from the surgeon's point of view, the most vital phenomenon accompanying shock is a low blood-pressure, we concluded at that time that the most important effect of traumatism as it is related to practical surgery is the impairment of the vasomotor mechanism. It was soon apparent, however, that this conception did not adequately explain all the phenomena of shock.

We then investigated various methods by which shock might be prevented, and found that the shock phenomena did not follow trauma, however prolonged or intense, in territories the nerve-supply of which was blocked; that shock during operation or injury was conspicuously diminished by morphin administered hypodermically prior to the operation or injury, and by local

[1] G. W. Crile: An Experimental Research into Surgical Shock.

and regional anesthesia; that careful handling, sharp dissection, and minimum trauma, also, were effective in preventing shock.

These later investigations, published in 1901,[1] laid the foundation for the development of a preventive technic which we later designated anoci-association.

In our belief that one of the most vital effects of shock was low blood-pressure, we next directed our attention to the maintenance of the blood-pressure, and first investigated the drug stimulants in common use, such as alcohol, camphor, strychnin, nitroglycerin, digitalis. We were disappointed in finding that none of these drugs prevented or lessened shock, but that, on the whole, they predisposed to or increased shock. This was especially true in the case of strychnin, for we found that shock could be produced by strychnin alone, and that it was as illogical to treat traumatic shock with strychnin as it would be to treat strychnin shock with trauma.

We then endeavored to maintain the blood-pressure by applying pressure upon different parts of the body, and devised a pneumatic suit, by means of which the general blood-pressure could be raised at will within a range of from 15 to 45 mm. of mercury; but the suit was cumbersome and uncomfortable and was abandoned. We then sought to raise and sustain the blood-pressure by increasing the atmospheric pressure. Animals were placed in a metal cylinder within which the atmospheric pressure could be varied at will. We found that the atmospheric pressure was transmitted equally through all parts of the body, and that therefore the general blood-pressure could not be increased by this means. By connecting the pulmonary tract with the external air while the body of the animal remained within the metal cylinder blood was easily thrown into the

[1] G. W. Crile: An Experimental and Clinical Research into Certain Problems Relating to Surgical Operations.

heart and lungs, and the blood-pressure raised and well sustained; but this required a cumbersome apparatus and the heart was easily overloaded.

Having failed to establish any valuable therapeutic action in drugs, in direct mechanical pressure on the body, or in increased air pressure, we turned to the treatment of shock by means of infusions. Since the preceding experiments proved that in shock the heart was but little impaired, it would appear that a volume of fluid sufficient to fill the vascular system might give the heart the opportunity to circulate the blood, and thereby overcome the damaging anemia of the brain.

We found that Locke's and Ringer's solutions and saline solution raised the blood-pressure only temporarily, and, moreover, that whatever the rate of infusion, the hemoglobin estimation and the red-blood-cell counts showed that the blood was not materially diluted. Moreover, after sufficiently large infusions the animals died in from five to eight minutes. The solutions passed through the vessel walls as fast as they entered. The abdomen distended rapidly and became hard and tense. The fluid accumulated in the walls and lumina of the stomach and the intestines, in the liver, and in the spleen, thus mechanically fixing the diaphragm and floating ribs, so that death was caused by asphyxia.

We then investigated the effects of adrenalin, and found that by employing a continuous intravenous infusion of a 1 : 50,000 solution of adrenalin at the rate of 3 c.c. per minute it was possible to maintain the blood-pressure for many hours. By this means the circulation in a decapitated dog was maintained for eleven hours. Adrenalin infusions were found effective in human cases, but the obvious difficulties and dangers in its use led us to continue the search for a better therapeutic agent by means of which the blood-pressure could be maintained. Later

researches showed that the excessive administration of adrenalin in itself causes exhaustion.

From these observations we concluded that the ideal treatment of shock would be to fill the blood-vessels with some fluid which would not pass through the vessel walls, would cause no chemical injury, would carry oxygen, and would always be immediately available. *Human blood is the only fluid which possesses all these qualities.* We therefore sought for a method by which the circulations of two animals could be so connected that blood could be transmitted at will from one to the other. At first we used glass cannulæ and rubber tubing, but clotting interfered. Then we used the Carrel suture technic, which was excellent, but technically too difficult for general use. Finally, a special connecting cannula was devised. We found that the transfusion of blood raised and maintained the blood-pressure more efficiently than any other agent we had tried. An *overtransfused* animal could even be decapitated without resultant change in its blood-pressure, provided artificial respiration was maintained. If an animal was overtransfused one day and decapitated the next its blood-pressure did not fall. These experiments showed that the elasticity of the overdistended blood-vessels supplied the normal peripheral resistance.

We then believed we had found a specific for shock, but further experimental research and clinical experience soon demonstrated that blood transfusion had certain limitations. In the clinic we found that transfusion was specific for hemorrhage, and was useful, although not specific, in shock, but that it was of no value in prostration from infections, in uremia, in cachexia, in prostration from exophthalmic goiter, in acute acidosis. In the laboratory we found it was of no value in hydrochloric acid poisoning, in too long deferred resuscitation, in anaphylactic shock, in collapse from iodoform-poisoning, or in the presence of amino-acids; it

did not benefit animals whose adrenals or whose livers had been excised; it was of no value in strychnin-poisoning or in prostration from excessive adrenalin injection, or excessive thyroid administration. *In fact, we were able to kill animals by traumatic shock while their blood-pressure was maintained at about 100 mm. mercury.* From these disappointing findings we drew two conclusions: (1) That until a more assured means of treatment was established the *prevention* of shock offered a more fruitful field for investigation; (2) that our search for the cause of shock and exhaustion must be carried much further.

We had previously observed in our experiments that the use of local or spinal anesthesia prevented shock from trauma of the blocked area. In 1900 Lower made use of spinal anesthesia in an amputation of the thigh for the purpose of preventing shock in an elderly man with a crushed leg. This is the first operation, as far as we know, in which spinal anesthesia was used for the purpose of preventing shock by blocking afferent impulses. Our expectations were fully realized. There was no change in the pulse-rate and the patient recovered.

These clinical observations and our laboratory researches suggested that in shock the brain cells may show morphologic changes analogous to the changes seen by Hodge in the nerve-cells of bees and birds. To this end Dr. D. H. Dolley, who was then associated with us in the laboratory, was asked to make a histologic study of the brains of dogs subjected to traumatic shock and of rabbits subjected to emotional shock. For nine years, with painstaking care, these nerve-cell investigations have been continued by Dr. J. B. Austin. As will be seen in the following chapters it has been found that the brain-cell changes give an excellent index to the degree of shock, not only of shock or exhaustion from trauma and from emotion, but of drug shock, toxic shock, anaphylactic and foreign protein shock—in fact, of all the forms of shock or exhaustion we have studied.

Believing that the changes in the brain cells were work changes, we then studied other organs whose functions seemed to indicate that they were closely related to the brain in its activities. And, finally, we threw out a net of inquiry so as to include every tissue and organ of the body, and found that in exhaustion from insomnia, from muscular exertion, from emotional excitation, from physical injury, from anaphylaxis, from electric stimulation, from the electric discharge of electric fish, from asphyxia, from starvation, from adrenalectomy, from the intravenous injection of acids, from prolonged inhalation anesthesia, from the intravenous injection of excessive amounts of adrenalin, from infection—in short, in exhaustion from any cause whatsoever—histologic changes in the brain, the liver, and the adrenals appear within from two to eight hours.

From the fact that the cellular changes are apparently identical, whether produced by the injection of acids, by interference with oxidation or by excessive oxidation, and from evidence to be shown later, it would seem that a state of intracellular acidosis exists in exhaustion. We found that acidosis was produced by many causes, and—a most striking and illuminating fact—that inhalation anesthetics cause acute acidosis. This suggested studies of acidosis in its relation to shock and exhaustion, which were undertaken in collaboration with Dr. M. L. Menten, and later a research on the reserve alkalinity, which was investigated in our laboratory by the method of Van Slyke by Drs. W. H. Crozier, W. B. Rogers, and B. I. Harrison. When we found that acute acidosis was present in all cases of shock, and that the alkali reserves were reduced, we hoped that the work of Howell and of Seelig had indicated the long-sought specific—viz., the administration of sodium bicarbonate. But once again we were disappointed, as alkalinization resulted in only a temporary improvement, although as it seems to have some therapeutic value, we use in the clinic a 5 per

cent. solution of sodium bicarbonate with 5 per cent. glucose as a routine rectal tap in cases in which exhaustion is present or threatened.

In the progress of these researches Drs. A. B. Eisenbrey, F. W. Hitchings, and C. H. Lenhart had found that in shock the blood was concentrated, but this finding was of no therapeutic value, since the transfusion of an abundance of unconcentrated blood does not cure.

Having noted that fundamental restoration occurred during rest, warmth, and sleep, we then turned our attention to a study of sleep. We had previously found that a sufficient loss of sleep causes intracellular lesions identical with those found in shock. We now found that these intracellular lesions are magically repaired during sleep. When we find the physico-chemical process by which sleep is produced, then, provided this process can be reproduced at will, we shall have the ideal treatment of shock and exhaustion.

From the beginning of our investigations to the present time the observations of the clinic and the findings of the laboratory have paralleled and controlled each other. Of the greatest possible value has been our continuing experience with exophthalmic goiter, since in this disease normal and pathologic physiologic phenomena are magnified.

We have found that the clinical phenomena of shock and exhaustion, whatever the exciting cause, are fundamentally the same, and our researches have indicated that the histologic changes in shock and exhaustion from any cause are identical.

It has long been evident that the word *shock* is a loose and unscientific term. We realize that it could well be dispensed with and the word *exhaustion* substituted. There is no clearly defined difference between exhaustion from this or from that cause. Whether an intracellular acidosis is established in the brain cells as the result

of an excessive functional activity which forms acid by-products faster than they can be eliminated, as is the case in excessive exertion, excessive physical injury, excessive emotion, excessive infection, excessive electric stimulation, excessive adrenalin stimulation; whether the intracellular acidosis is caused by lack of oxygen, as in asphyxia, in gas-poisoning, in imperfect circulation, in excessive hemorrhage; whether the intracellular acidosis is caused by the intravenous injection of acids; or whether the acidosis is due to a disturbance of the physiologic equilibrium of the cell by adrenalectomy, or excision of the liver, the ultimate result is the same, and the fundamental factors which accomplish restoration are the same.

We have come to look upon shock as an interference with the most fundamental mechanism of life—an interference with the mechanism for the transformation of energy. We have seen that extremely diverse factors are synergistic in the production of shock; that in general the causes of shock may be roughly divided into two groups, one comprising those in which an excessive energy transformation leads to intracellular acidosis, the other including those which cause intracellular acidosis and interference with internal respiration without an excessive transformation of energy. We have, therefore, designated our interpretation of shock the *Kinetic Theory of Shock.*

The kinetic theory of shock is no stronger and no weaker than the effectiveness of the means of prevention and treatment which are based on its postulates. The great war has given the authors the opportunity of testing the theory and the practice of anoci-association for themselves on a vast scale, and of seeing it tested by others, and it is because of the clean-cut confirmation of the theory in the crucible of this vast clinic that we set forth in another edition the principles upon which the theory is founded and their practical application.

CHAPTER I

THE KINETIC THEORY OF SURGICAL SHOCK

When a barefoot boy steps on a sharp stone there is an immediate discharge of nervous energy in his effort to escape from injury. This is not a voluntary act. It is not due to his own personal experience (his ontogeny), but is the result of the experience of his progenitors during the vast periods of time required for the evolution of his species (his phylogeny). The wounding stone made an impression upon the nerve receptors in the foot similar to the innumerable injuries, as a result of which this nerve mechanism itself was evolved during the boy's vast phylogenetic or ancestral experience. The stone supplied the phylogenetic association and the required discharge of nervous energy automatically followed.

In like manner all actions are performed. Every adequate stimulus awakens an ontogenetic or phylogenetic memory or *association,* and the nerve mechanism evolved by countless similar experiences in the life of the individual or of his race makes the adequate response. These *associations,* like that awakened by the sharp stone in our illustration, may be injurious to the individual —*noci-associations;* or they may be of benefit to the individual —*bene-associations.* The sight of appetizing food is a *bene-association;* it awakens both the phylogenetic and the ontogenetic memory of similar experiences. The nerve centers are stimulated as if the food were actually being eaten, and the "mouth waters."

All of life, therefore, is made up of *bene-* and *noci-associations,* and the constant effort of the individual and of the race is to increase the former and decrease the latter, to develop an environ-

ment which shall, as far as possible, be free from *noci-associations* —to reach a state of *anoci-association.*

The environmental influences that threaten annihilation, such as the assaults of beasts or of man against man; the impacts of sharp, rough, and moving objects; the irritations of dust and débris, are among the coarser, *nocuous* elements, to meet which there have been evolved in man adaptive mechanisms which are excited to activity by the *noci-ceptors,* which are richly implanted in the skin and in other parts and organs. The nocuous effects of cold, rain, and storm are met by other adaptations—shelter, clothing, and fire; while against those unseen nocuous elements which cannot be perceived by the senses—pathogenic bacteria—the body has evolved chemical defenses—antibodies, immunity, febrile reaction, phagocytosis.

Thus man is constantly beset by *noci-associations* and as constantly is striving to reach a state of *anoci-association.* An umbrella in a rain-storm; a glowing fireside in a blizzard; bolts and bars against attack; antitoxin in infection—all are attempts to produce *anoci* conditions. In the beginning of human history, however, man in common with most animals had two principal methods of self-defense against the dangers which surrounded him—he fought or he ran away.

There is strong evidence that the animals most capable of being shocked are those whose self-preservation originally depended upon some form of motor activity. In man and other animals this motor activity expresses itself in running and fighting; hence the motor mechanism comprises the muscles and the organs that contribute to their activity.

Motor activity, then, is excited by the adequate stimulation of the nerve ceptors, both of the *contact* ceptors in the skin and of the *distance* ceptors or special senses. We assume that excessive stimulation of the distance ceptors (special senses) is as potent

as excessive stimulation of the contact ceptors in producing shock. As has already been indicated, we assume also that the environment of the past (phylogeny), through the experiences of adaptation to environment, predetermines the environmental reactions of the present. It is, therefore, the motor mechanism in particular which through its phylogenetic association with injury to the individual is responsible for the discharges of energy which are occasioned by the presence or even the thought of danger. These stimuli, when intense enough or protracted enough, produce the extreme conditions called "exhaustion" and "shock." In other words, this type of shock is caused by *excessive stimulation of the mechanism of energy transformation.*

Stimuli of sufficient number or intensity inevitably cause exhaustion and may cause death. If the functional activity of the brain cells, resulting from responses to stimuli, takes the form of obvious work performed, such as running, the phenomena expressing the depletion of the vital force are termed *physical exhaustion.* If the stimuli are so intense that the brain cells become so damaged as to be unable to perform their work, the condition is commonly designated *shock.*

While the precise nature of the change in the brain cells is not known, Eisenbrey and DeEds in my laboratory in France showed that in exhaustion the function of the brain cells was impaired before the blood-pressure fell; and in our electro-chemical researches here, in collaboration with Miss Hosmer, we found a decreased conductivity of the brain in exhaustion from any cause.

Surgical shock, therefore, may be produced by divers causes, such as fear and worry, physical injury, infection. Moreover, since in shock the internal respiration is depressed, a predisposition to shock may be produced or the shock may be augmented by other causes of interference with internal respiration, such as hemorrhage, asphyxia, anemia, starvation, loss of sleep, etc.

We shall present evidence that these conditions cause physical alterations in the cells of the brain, the liver, and the adrenals; that these physical changes are identical, whatever their cause; and that those cells of the brain which reach a certain degree of alteration cannot be restored, and their deterioration goes on to destruction. The histologic changes in the brain, the liver, and the adrenals may be caused by emotion alone, by physical injury alone, by hemorrhage alone, by starvation alone, by insomnia alone, by adrenalectomy, by excessive adrenal injection, by excessive thyroid feeding, by the injection of acids, etc.; or these changes may be initiated by emotion, carried a step further by muscular exertion, another step by physical injury, another by hemorrhage, and so on until many brain cells are destroyed; or all these factors acting simultaneously may produce the same disastrous result. There is no microscopic evidence of specificity in the effects of these various factors; that is, no one could look at an altered brain cell, an altered liver cell, or an altered adrenal cell under the microscope and be able to state the cause of its structural change. *These changes in shock and in exhaustion from any cause whatsoever seem to be identical.*

Among the multitude of causes of exhaustion, with their identical clinical and pathologic phenomena, we shall in this monograph deal mainly with those causes that play a rôle in the outcome of surgical operations and injuries. We shall consider first the pathology of traumatic shock, of emotional shock, of toxin and foreign protein shock, and then the practical application of the *kinetic theory of shock* in the development of the shockless operation through *anoci-association*—or *anociation*.[1]

[1] Hereafter the shorter but equally significant term *anociation* will be used in preference to the original *anoci-association*.

CHAPTER II

THE CAUSE AND PATHOLOGY OF SURGICAL SHOCK

In general we may divide the chief causes of surgical shock into two groups, arbitrarily designated as predisposing causes and exciting causes.

An individual may be predisposed to surgical shock by diverse causes, such, for example, as infancy and old age; chronic debilitating diseases, such as pernicious anemia, myocarditis, broken cardiac compensation, advanced malignant disease, diabetes, tuberculosis, cardiorenal and cardiovascular disease; exophthalmic goiter and myxedema; partial starvation from obstruction of the alimentary tract, *i. e.*, of the esophagus, pylorus, or colon; cirrhosis or tumor of the liver; obstruction of the common bile-ducts; interference with pulmonary ventilation, *i. e.*, partial obstruction of the larynx or trachea, emphysema, tumors of the lung, the pleura, or the mediastinum; pregnancy, eclampsia, chronic hemorrhage, such as pathologic hemorrhage from the kidney or rectum or uterus; all the acute or chronic infections; excessive exertion, loss of sleep and cold; and ether and chloroform anesthesia.

Clinical experience and experimental research show that when, the organism is partially reduced by any of these predisposing causes the emotional and traumatic factors of a surgical operation will be brought to play against a correspondingly reduced margin of safety, and the state of exhaustion or shock is the more readily reached.

Perhaps the real distinction between the predisposing causes of shock included in the foregoing list and the exciting causes is the fact that the predisposing causes exert their unfavorable action on the patient before the beginning of the surgical operation.

Under our conception a surgical operation includes not only the instruments and manipulations of the surgeon but also the intellect and the viewpoint of the surgeon. From this standpoint the one great exciting cause of surgical shock is the surgeon—every contact of his instrument with an unanesthetized nerve-ending, nerve-filament, or nerve-fiber; every drop of blood which he sheds; every moment he requires the continuation of inhalation anesthesia; every moment he exposes sensitive tissue to the air; every interference with adequate ventilation of the lung; every thrill of fear he introduces into his patient—each of these is an exciting cause of shock, and the combined result of all may be death.

Any *one* of the exciting causes of shock mentioned above may in itself cause death; certain of the basic phenomena of death from one exciting cause are identical with the basic phenomena of death due to any combination of exciting causes; certain of the basic phenomena of death due to one or more exciting causes are identical with the phenomena of death from one or more predisposing causes; and, finally, certain basic phenomena of death from a combination of predisposing and exciting causes are identical with the corresponding phenomena of death from one or more exciting causes alone, or from one or more predisposing causes alone. In other words, *in the mechanism of death from shock there is no factor which distinguishes that death from death from many other causes.*

A study of shock is merely a study of one group of *conspicuous death-dealing causes;* and it is also a study of every-day life processes when they are driven rapidly to a breakdown.

The predisposing and exciting causes of shock, then, are merely intensifications and combinations of every-day causes of fatigue and death; but it so happens that so abnormal a biologic state as the mechanical injury incident to a surgical operation has a peculiar facility for achieving fatigue or death.

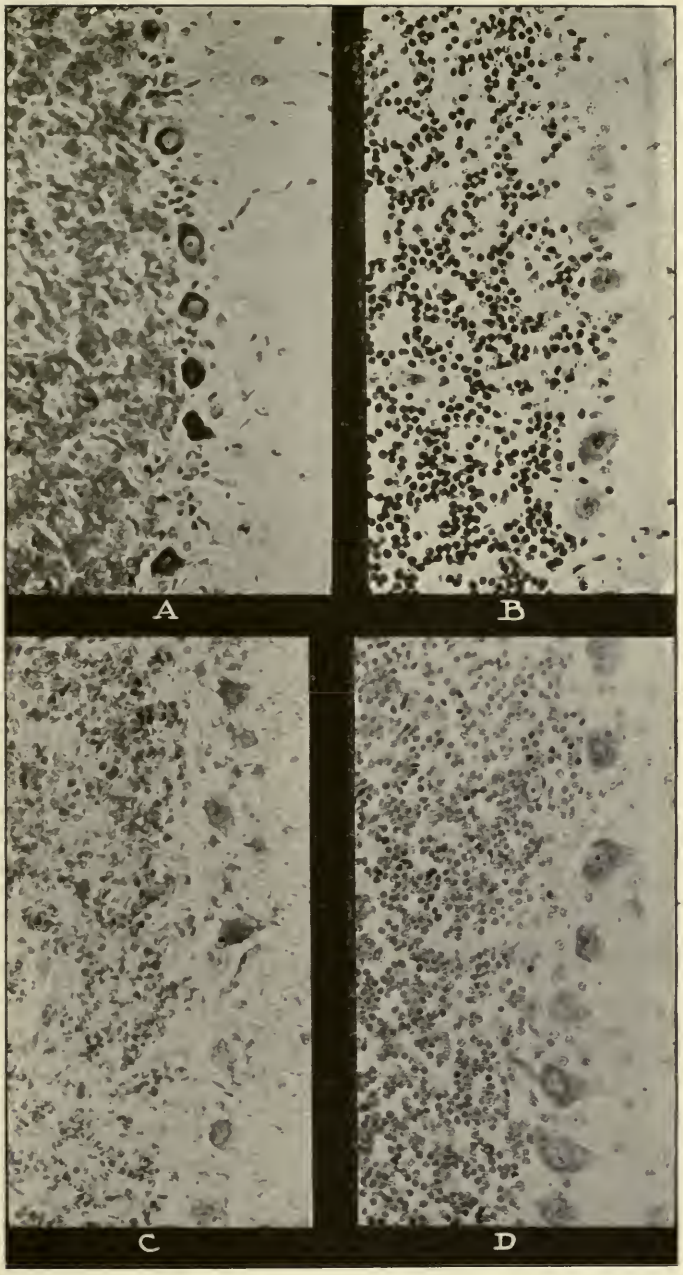


FIG. 1.—HISTOLOGIC CHANGES PRODUCED IN THE BRAIN BY PHYSICAL EXERTION, INFECTION, AND SKATOL (AUTO-INTOXICATION). (From photomicrographs × 310.)

A, Section of normal cerebellum of a cat. B, Section of cerebellum of a cat which had been subjected to extreme and prolonged physical exertion. C, Section of cerebellum of a cat after streptococcal infection. D, Section of cerebellum of a cat which had received repeated injections of skatol.

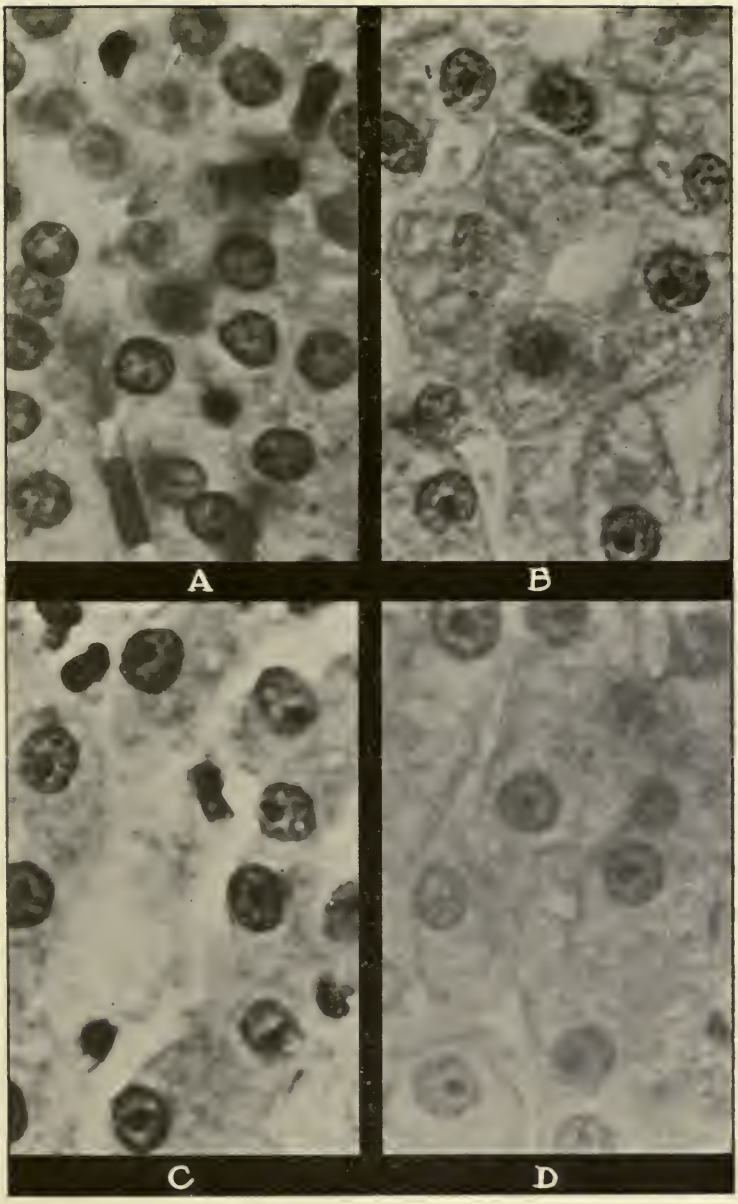


FIG. 2.—HISTOLOGIC CHANGES PRODUCED IN THE LIVER BY PHYSICAL EXERTION, INFECTION, AND SKATOL (AUTO-INTOXICATION). (From photomicrographs × 1640.)

A, Section of normal liver of a cat. B, Section of liver of a cat which had been subjected to extreme and prolonged physical exertion. C, Section of liver of a cat after streptococcal infection. D, Section of liver of a cat which had received repeated injections of skatol.

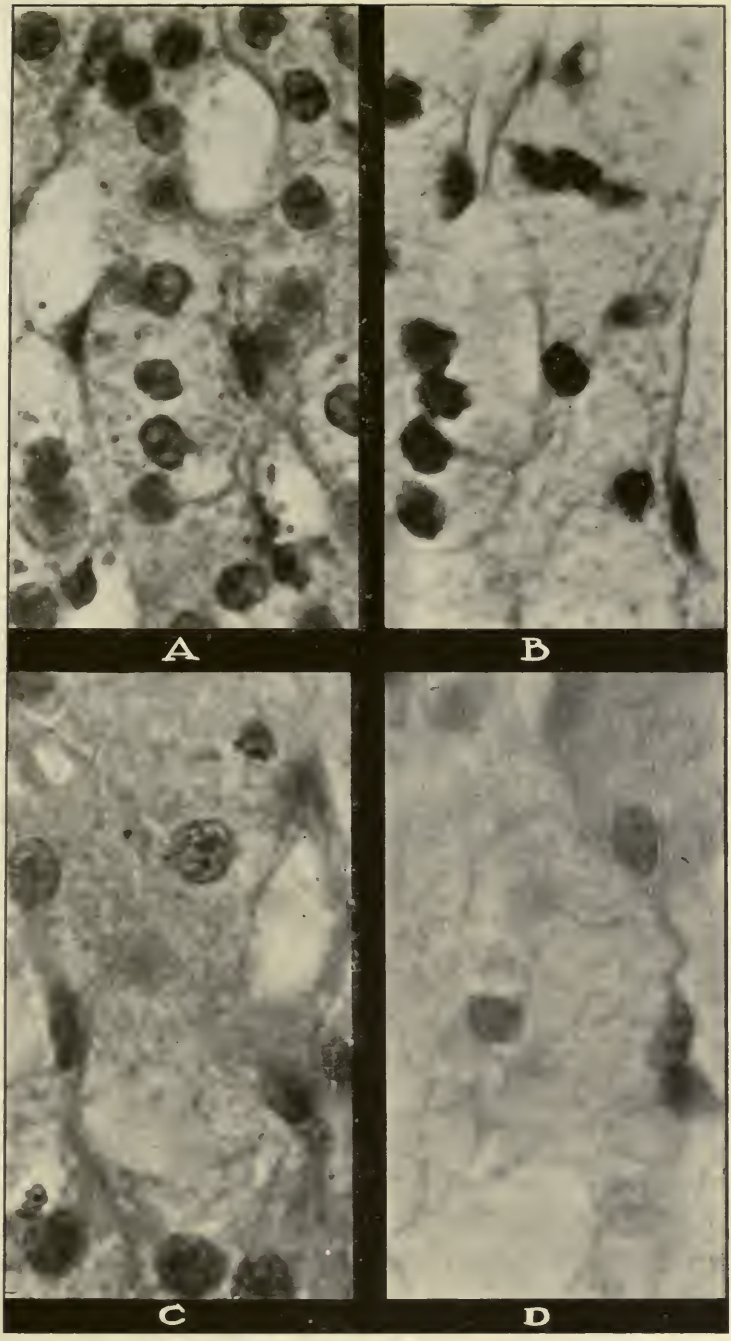
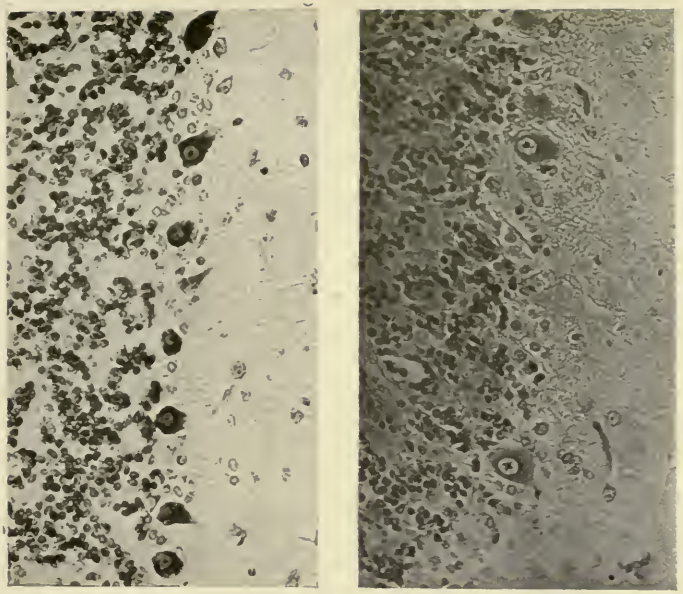
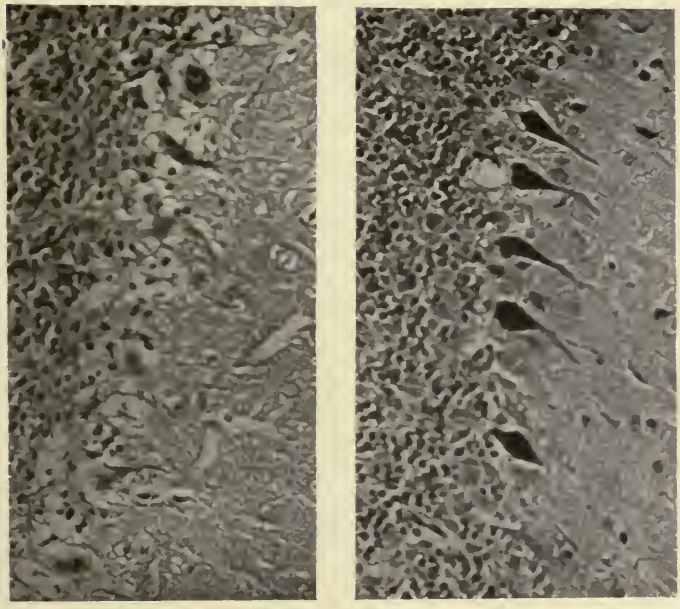


FIG. 3.—HISTOLOGIC CHANGES PRODUCED IN THE ADRENALS BY PHYSICAL EXERTION, INFECTION, AND SKATOL (AUTO-INTOXICATION). (From photomicrographs × 1640.)

A, Section of normal adrenal of a cat. B, Section of adrenal of a cat which had been subjected to extreme and prolonged physical exertion. C, Section of adrenal of a cat after streptococcal infection. D, Section of adrenal of a cat which had received repeated injections of skatol.



A B



C D

FIG. 4.—THE PROTECTIVE EFFECT OF SLEEP. (From photomicrographs × 310.)

A, Normal cerebellum of a rabbit. B, Cerebellum of rabbit after injection of sodium acid phosphate. C, Cerebellum of rabbit after injection of sodium acid phosphate plus a period of insomnia. D, Cerebellum of rabbit showing the protective effect of normal sleep after injection of sodium acid phosphate.

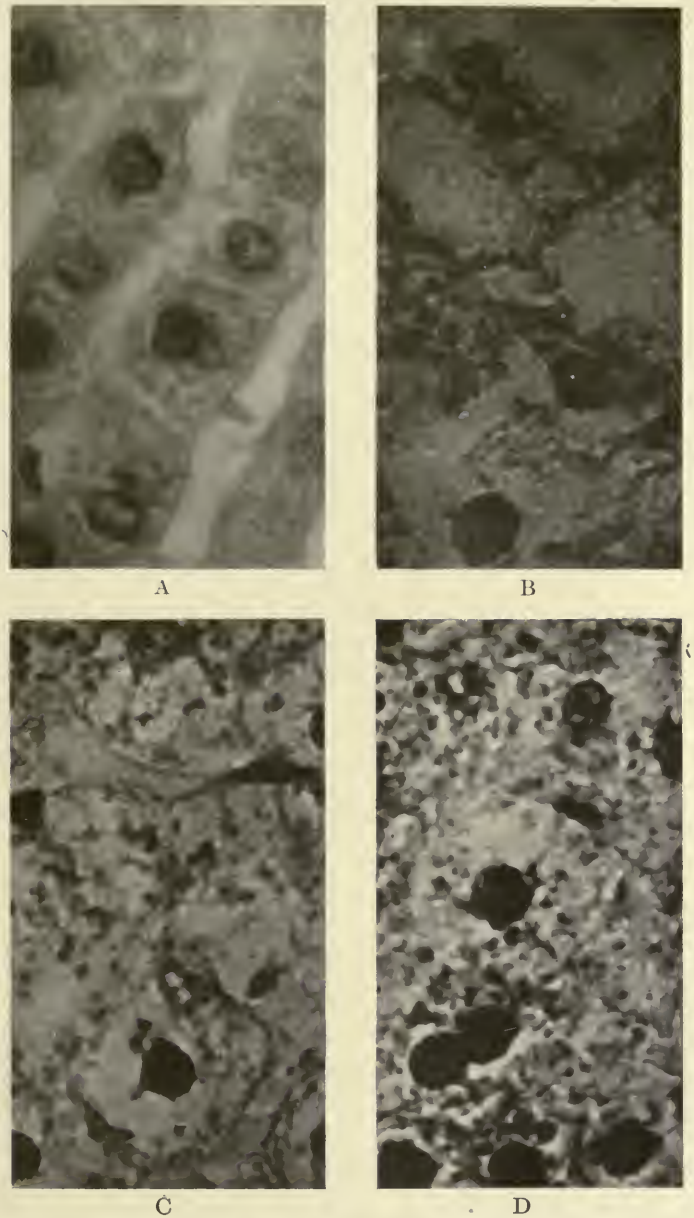


FIG. 5.—THE PROTECTIVE EFFECT OF SLEEP. (From photomicrographs × 1640.)

A, Normal liver of a rabbit. B, Liver of rabbit after injection of sodium acid phosphate. C, Liver of rabbit after injection of sodium acid phosphate plus a period of insomnia. D, Liver of rabbit showing the protective effect of normal sleep after injection of sodium acid phosphate.

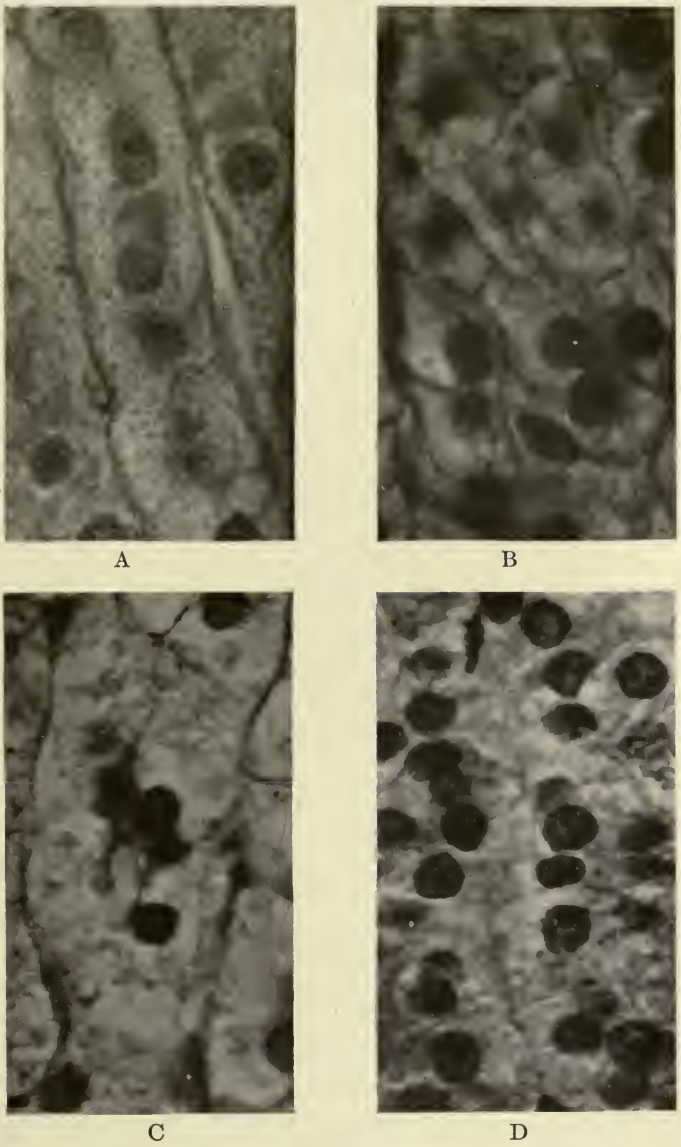


FIG. 6.—THE PROTECTIVE EFFECT OF SLEEP. (From photomicrographs × 1640.)

A, Normal adrenal of a rabbit. B, Adrenal of rabbit after injection of sodium acid phosphate. C, Adrenal of rabbit after injection of sodium acid phosphate plus a period of insomnia. D, Adrenal of rabbit showing protective effect of normal sleep after injection of sodium acid phosphate.

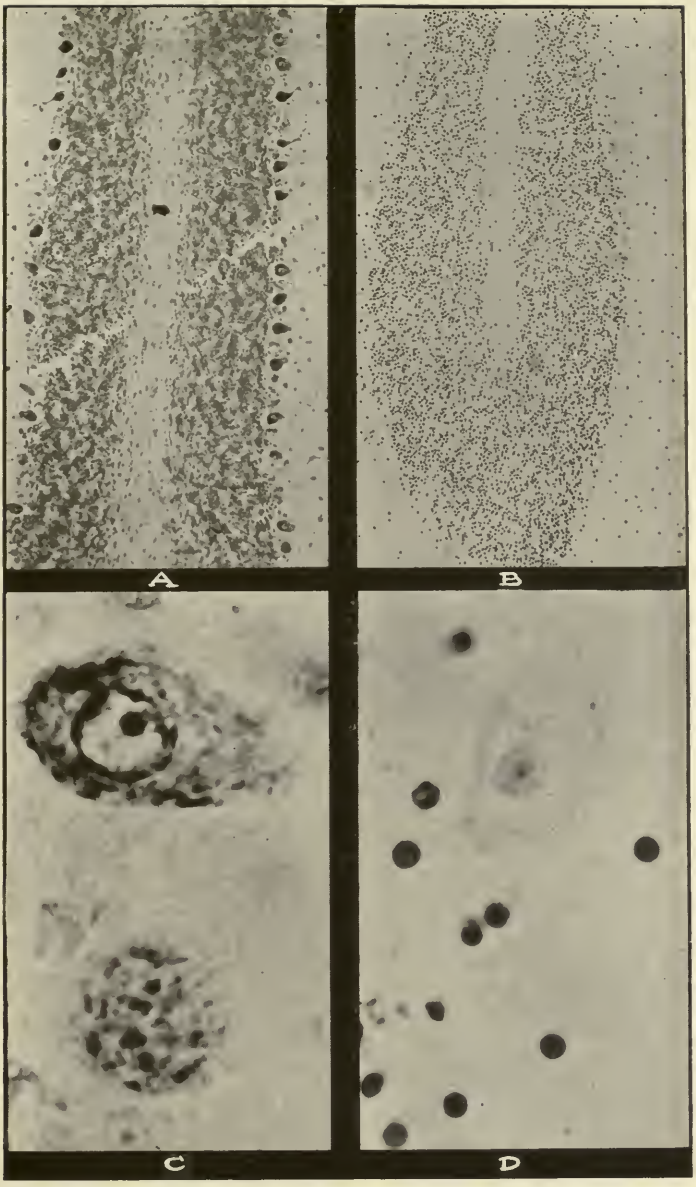


FIG. 7.—EFFECT OF INSOMNIA ON THE CEREBELLUM OF A RABBIT. (A and B from photomicrographs × 120; C and D from photomicrographs × 1640.)

A and C, Section from normal cerebellum of a rabbit. B and D, Section from cerebellum of a rabbit after insomnia for one hundred and nine hours Note the almost complete disintegration of the Purkinje cells in B and D.

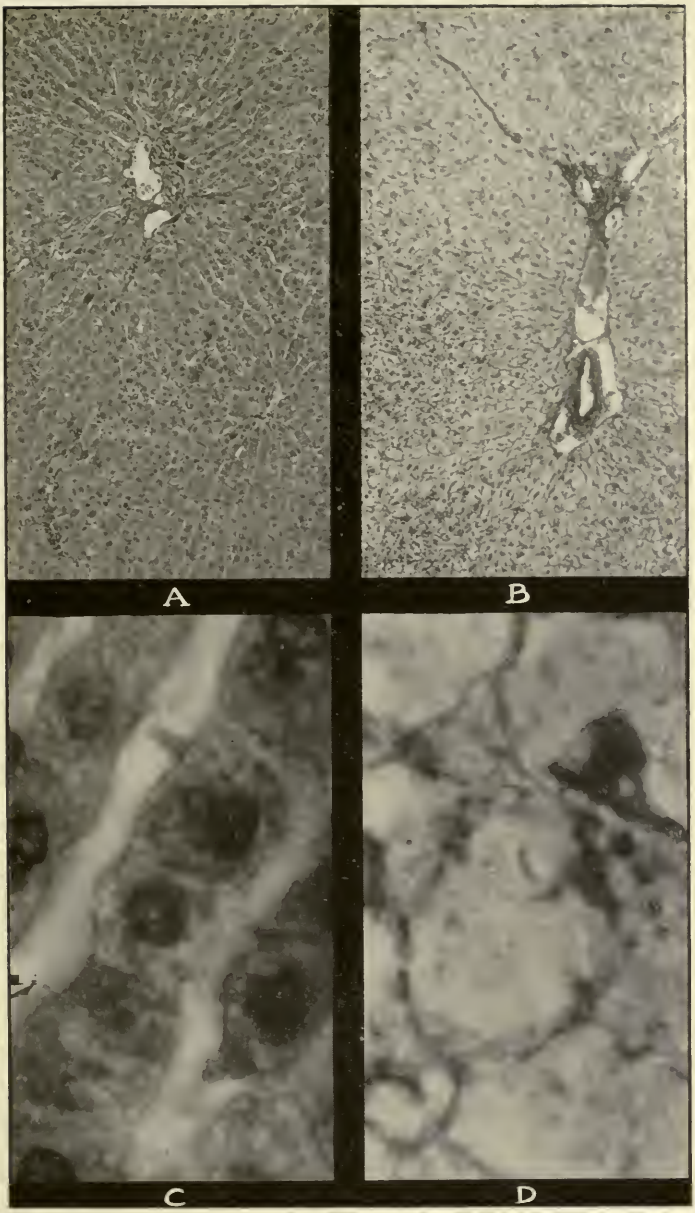


FIG. 8.—EFFECT OF INSOMNIA ON THE LIVER OF A RABBIT. (A and B from photomicrographs × 100; C and D from photomicrographs × 1640.)

A and C, Section from normal liver of rabbit. B and D, Section from liver of a rabbit after insomnia for one hundred and nine hours. Note the general loss of cytoplasm, the disappearance of nuclei, the vacuolation, and the swollen cells in B and D.

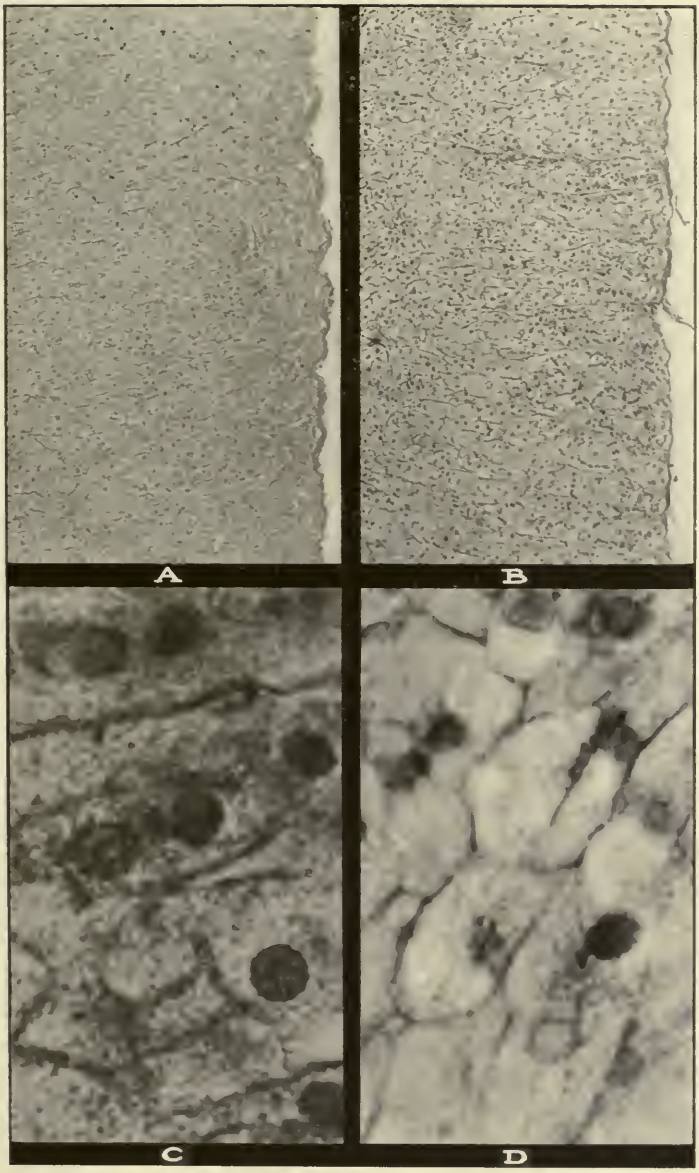


FIG. 9.—EFFECT OF INSOMNIA ON THE ADRENAL OF A RABBIT. (A and B from photomicrographs × 100; C and D from photomicrographs × 1640.)

A and C, Section from normal adrenal of rabbit. B and D, Section from adrenal of rabbit after insomnia for one hundred and nine hours. Note the general loss of cytoplasm, the disappearance of nuclei, and the distortion of the cell outlines in B and D.

The photomicrographs of slides included in the cytologic studies of one of our collaborators, Dr. J. B. Austin, show the identical lesions in exhaustion from various causes as revealed by the microscope (Figs. 1–3).

We have seen that exhaustion (shock) and death, with its intracellular changes, have many causes. How many causes of restoration are there? Our later researches have shown that whatever the cause of the intracellular changes in exhaustion, the real repair of these changes takes place mainly, perhaps only, during rest and sleep. In other words, the phenomena of sleep and the phenomena of repair are due to the same physico-chemical cause. There is, therefore, but one real source of restoration, rest and sleep—deep untroubled sleep. The photomicrographs show in a striking manner nature's restorative power by means of a process not yet more than glimpsed (Figs. 4–6).

What is the nature of the changes seen in the brain, in the liver, and in the adrenals? Can a man or an animal have normal muscular power and normal mental power when his brain cells are thus altered? We believe that the following negative statement is relatively correct; *i. e.*, that no animal—no man—can develop normal muscular or normal mental energy when the brain cells have undergone such intracellular changes as are shown in these photomicrographs. This statement is based on the vast labors of Dr. Austin in his histologic examination of more than 3000 animals and men. In not a single case of deep fatigue, exhaustion, or grave shock, in which life continued from three to eight hours, did Austin fail to find a histologic picture which varied in degree only from that shown in the photomicrographs (Figs. 7–9); on the other hand, in not a single normal animal did he find such a microscopic picture as that seen in exhaustion.

We are forced to conclude that the intracellular changes express a physico-chemical disturbance which constitutes a definite pathol-

ogy of shock, the ultimate explanation of which must be deferred until the normal process of life is further explained.

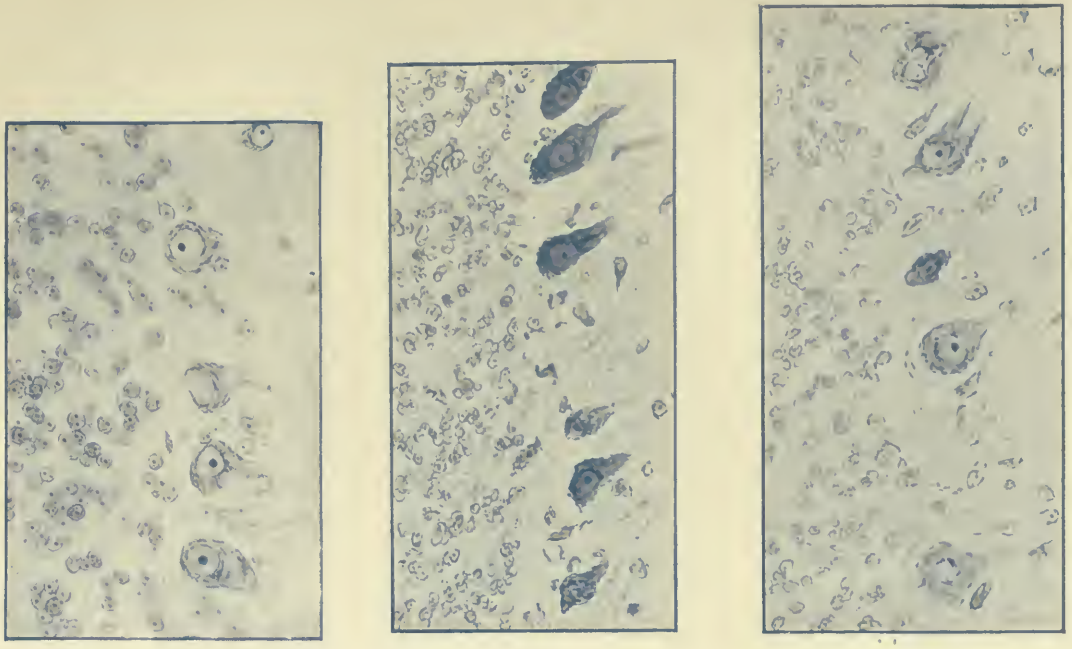
Having established a pathology of shock, we then had in our possession one more criterion for a fairly accurate judgment of (*a*) the relative effect of this or of that cause of shock; (*b*) the relative value of this or of that method of treatment.

Combining these pathologic studies by Dr. Austin with physiologic studies by Drs. Sloan and Hitchings; with studies of the H-ion concentration of the blood and of the reserve alkalinity by Drs. Menten, Crozier, Rogers, and Harrison; with a study of those causes of shock associated with increased output of adrenalin by Drs. Hitchings and Mosiman; with studies of the glycogen content of the liver and muscles and of the iodin content of the thyroid by Messrs. Biggs, Hamilton and Rome of the Parke-Davis Laboratories, with measurements of the electric conductivity of the brain, liver, and other tissues by Dr. J. B. Obear and Miss Helen R. Hosmer, and finally with our own clinical experience, we found that the kinetic theory was in harmony with the facts.

TRAUMATIC SHOCK

When physical injury alone was inflicted on normal dogs under inhalation anesthesia a certain number of the brain cells showed first a stage of hyperactivity characterized by hyperchromatism; and later a stage of exhaustion characterized (*a*) by chromatolysis; (*b*) by alteration of nucleus plasma relation; (*c*) by rupture of the nuclear and the cell membranes; and finally (*d*) by disintegration (Fig. 10). These changes were most marked in the cortex and the cerebellum, but were present also in the medulla and the cord.

The brain cells showed no change when the trauma was limited to territories disconnected from the brain by severing the spinal cord or by local anesthetization (Figs. 11, 12). When the circulations of two dogs were crossed and but one dog was traumatized,



A B C

FIG. 10.—BRAIN CELLS SHOWING STAGE OF HYPERCHROMATISM FOLLOWED BY CHROMATOLYSIS RESULTING FROM THE CONTINUATION OF THE STIMULUS. (From camera lucida drawings.)

A, Area from normal cerebellum of rabbit. B, Area from cerebellum of rabbit after single dose of strychnin. C, Area from cerebellum of rabbit after repeated doses of strychnin.

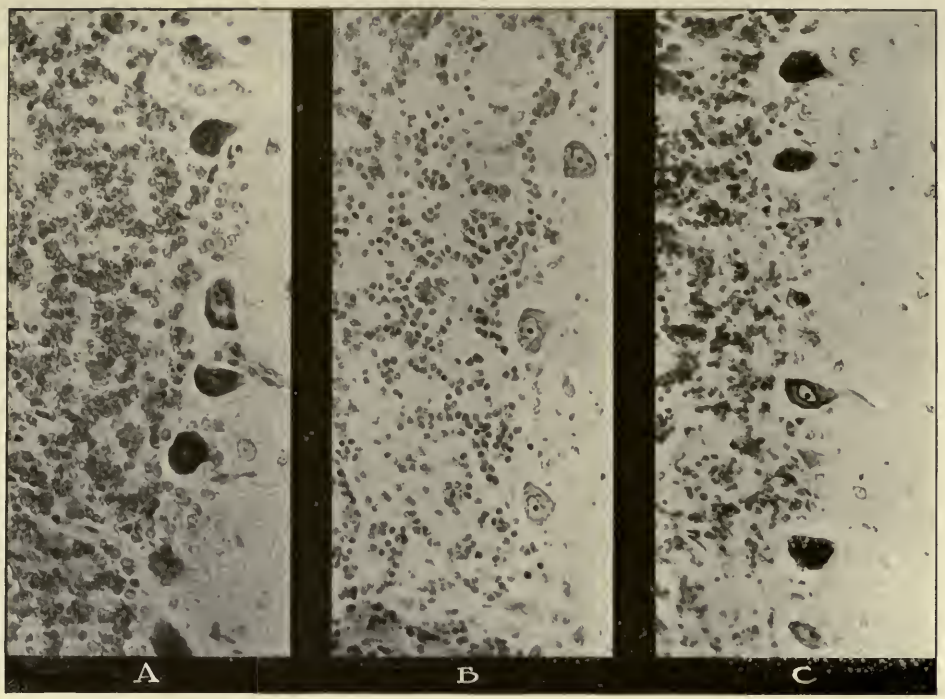
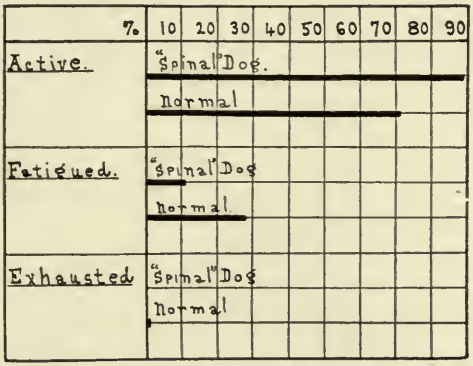


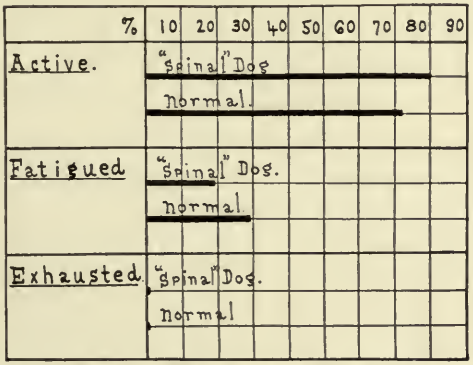
FIG. 11.—COMPARISON BETWEEN THE EFFECTS OF SURGICAL TRAUMA ON THE CEREBELLUM OF A NORMAL DOG AND ON THE CEREBELLUM OF A DOG WHOSE CORD HAD BEEN SEVERED. (From photomicrographs × 310.)

A, Section of normal cerebellum of a dog. B, Section of cerebellum of a dog which had received severe surgical trauma. C, Section of cerebellum of a dog which received severe surgical trauma after the spinal cord had been severed.

brain-cell changes were found only in the dog traumatized. Dogs overtransfused—to eliminate the factor of anemia—and trauma-



Attempted shock of a dog immediately after severing the spinal cord at the seventh cervical vertebra.



Attempted shock of a dog two and one-half months after severing the spinal cord at the seventh cervical vertebra.

The dog's spinal cord was severed at the seventh cervical vertebra, recovery following after a stormy convalescence. At the end of two and one-half months the dog was given ether, and severe shock-producing manipulations were carried on for four hours. At the beginning and end of the experiment, burning both a front and a hind paw caused practically no vasomotor reaction. Moreover, at the end of the experiment the blood-pressure had fallen only 8 mm. of mercury. Examination of the cord at the point of division showed only fibrous tissue. A differential Purkinje cell count showed hyperchromatism and no fatigue or exhaustion of consequence. Hence the shock-producing afferent impulses were blocked by the break in the cord and no shock was produced.

FIG. 12.—DIFFERENTIAL PURKINJE CELL COUNTS SHOWING THE PERCENTAGE OF ACTIVE, FATIGUED, AND EXHAUSTED CELLS IN "SPINAL DOGS" AFTER ATTEMPTS TO PRODUCE SHOCK BY TRAUMA.

tized showed brain-cell changes. When the vitality had been previously reduced by emotion, by physical exertion, by toxins, by

infection, by hemorrhage, by excessive thyroid feeding, by adrenalectomy—or by any cause that reduces the vital power—greater changes were found after equal trauma, the endurance of the animal being in proportion to its vitality at the beginning of the experiment. We found that trauma under curare caused no more brain-cell changes than approximately equal trauma under ether.

From these observations we conclude that ether anesthesia offers no protection to the brain cells against the effect of trauma, and that the *lipoid-solvent* anesthetics probably break the arc which maintains consciousness beyond the brain cells somewhere in the *efferent* path. *The afferent path from the seat of injury being unbroken, the afferent stimuli reach and modify the brain cells as readily as if no anesthetic had been given, and it would seem that the brain-cell changes must be due to the excessive stimuli which excited a futile effort to escape from the injury.*

EMOTIONAL SHOCK

In rabbits subjected to the emotional stimulus of fear alone, without accompanying trauma or muscular exertion, the brain cells show precisely the same changes as those which result from physical injury, that is, an immediate stage of *hyperchromatism* and a later stage of *chromatolysis;* a disturbance of the nucleus plasma relation, edema, and the final disintegration of many cells (Fig. 13).

In two experiments in which rabbits were subjected to intense fear daily—in one case for two weeks and in the other for three weeks—10 per cent. of the Purkinje cells were actually destroyed. In cats the emotion of rage caused a striking increase in the output of adrenalin (Fig. 14), but in cats subjected to fear and rage a month after the division of the major and minor splanchnic nerves there was no increase in the output of adrenalin. In rabbits acute fear caused a rise in temperature of from one to three degrees, except in thyroidectomized animals, whose temperature remained subnormal.

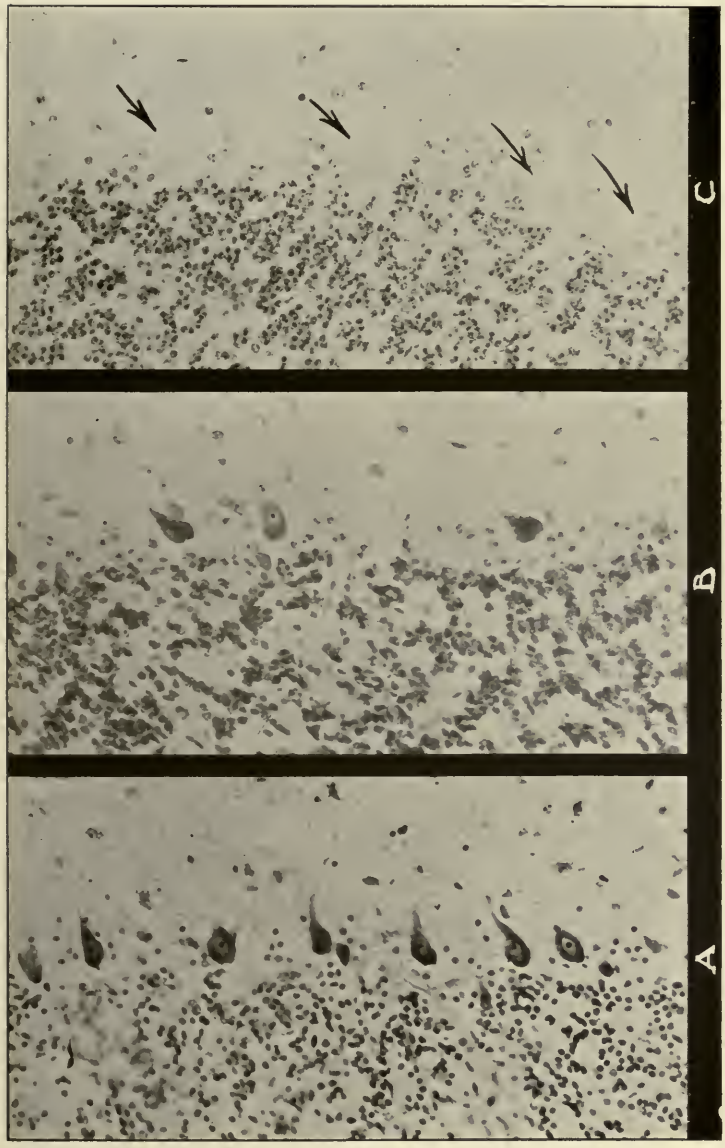


FIG. 13.—IMMEDIATE AND LATE EFFECTS OF FEAR ON THE CEREBELLUMS OF WOODCHUCKS. (From photomicrographs × 310.)

A, Section of cerebellum of a hibernating woodchuck. B, Section of cerebellum of a woodchuck killed immediately after one séance of fright. C, Section of cerebellum of a woodchuck killed four hours after one séance of fright. (Note the almost complete disintegration of the Purkinje cells indicated by arrows.)

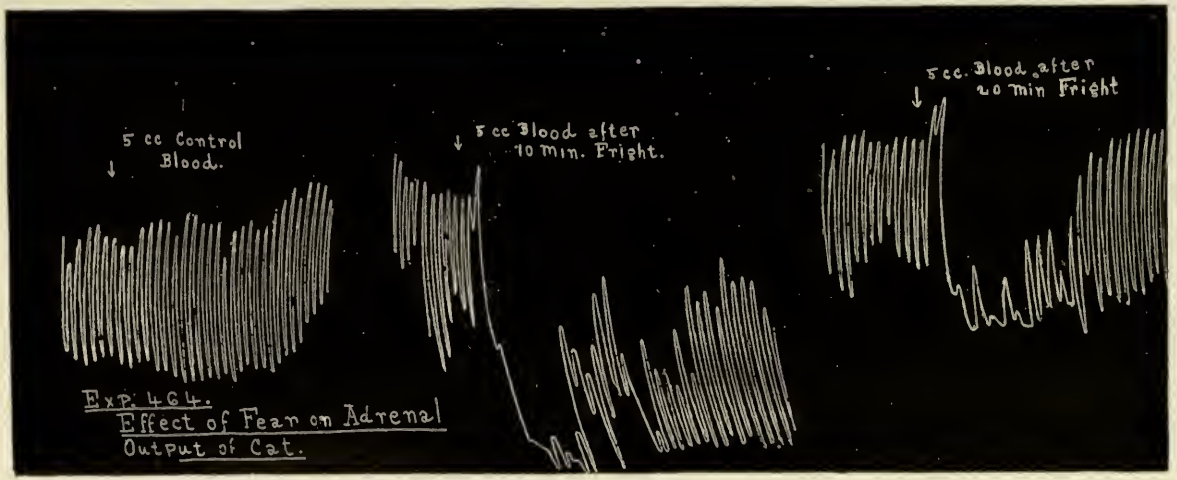
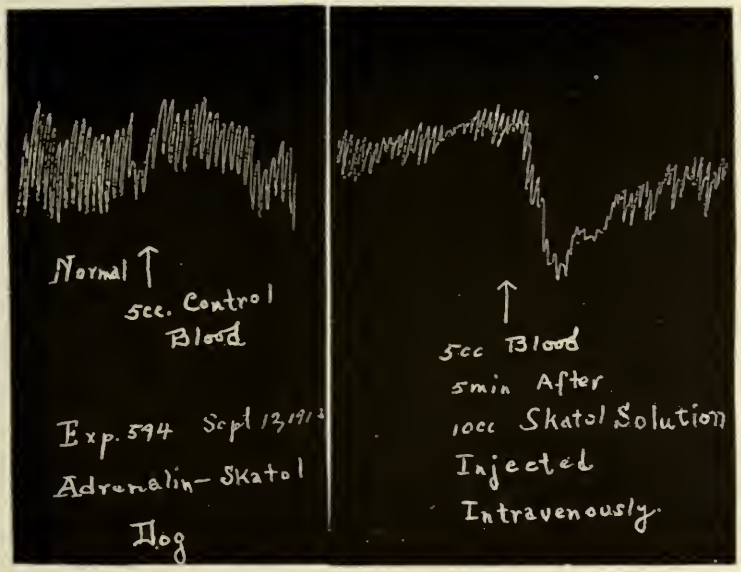


FIG. 14.—TRACING SHOWING EFFECT OF FEAR ON THE ADRENAL OUTPUT OF A CAT. (Cannon Test.)

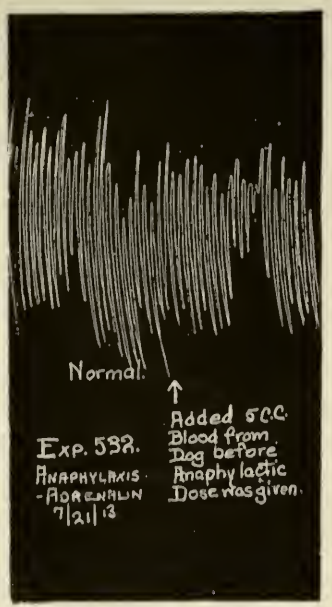
The first tracing (A) was made by the contractions of intestinal muscle in blood from a normal cat. The contractions of the intestinal muscle were inhibited when the normal blood was replaced by blood from the same animal after it had been frightened. This inhibition is evidence of increased adrenalin in the blood-stream, more adrenalin apparently being produced in the early stages of fright (B) than in the later stages (C).



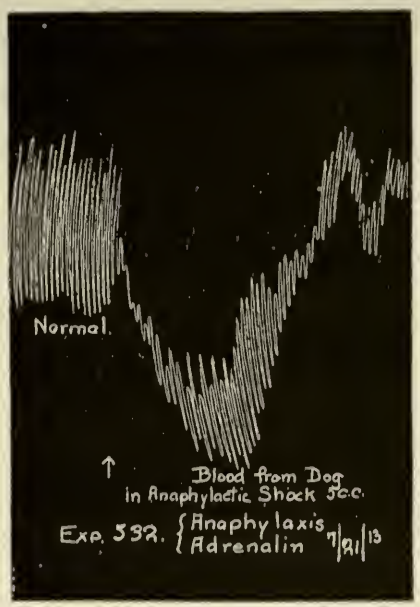
A B

FIG. 15.—TRACING SHOWING EFFECT OF SKATOL ON THE ADRENAL OUTPUT OF A DOG. (Cannon test.)

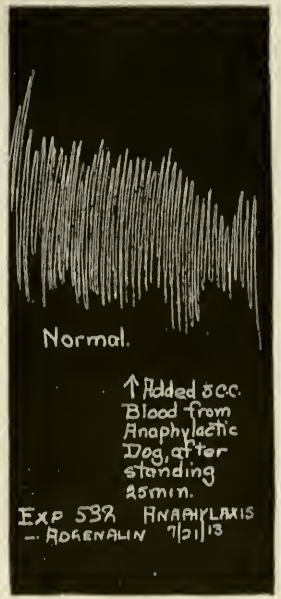
The first tracing (A) was made by the contractions of intestinal muscle in blood from a normal dog. The second tracing (B) shows the partial inhibition of the contractions produced by the substitution of blood after the injection of skatol, evidencing the presence in the blood of an increased amount of adrenalin.



Control test negative no adrenalin present.



Anaphylaxis test positive—that is, adrenalin has appeared in the blood and causes inhibition of the contraction of the intestinal segment.



Oxidation test negative (made by using a portion of the blood used for the anaphylaxis test after allowing it to stand for twenty-five minutes; the adrenalin has been oxidized and hence the inhibition is not repeated).

FIG. 16.—TRACING SHOWING EFFECT OF ANAPHYLAXIS ON THE ADRENAL OUTPUT OF A DOG. (Cannon test.)

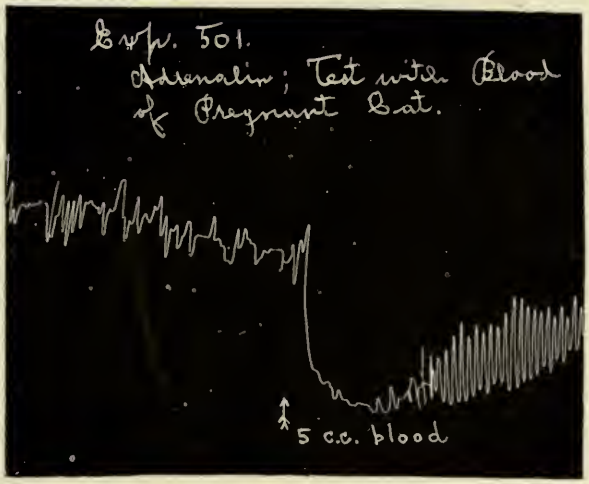
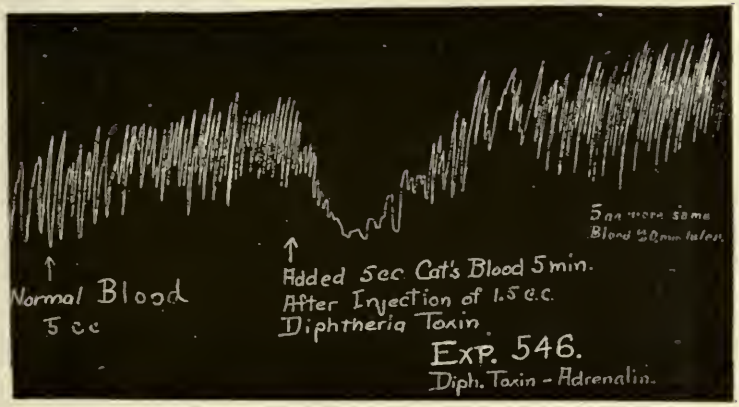


FIG. 17.—TRACING SHOWING EFFECT OF PREGNANCY ON THE ADRENAL OUTPUT OF A CAT. (Cannon test.)

That the adrenal glands are activated during pregnancy is demonstrated by this sharp inhibition of the contractions of intestinal muscle when the blood of a pregnant cat is substituted for normal blood.



A B C

FIG. 18.—TRACING SHOWING EFFECT OF DIPHTHERIA TOXIN ON ADRENAL OUTPUT OF A CAT. (Cannon test.)

The first tracing (A) was made by the contractions of intestinal muscle beating in blood from a normal cat. These contractions were inhibited almost entirely by the substitution of blood from the same cat after the injection of diphtheria toxin (B). After twenty minutes the increased adrenalin evidenced by B was oxidized and the intestinal muscle resumed its contractions as in normal blood (C).

TOXIC, FOREIGN PROTEIN, AND ANAPHYLACTIC SHOCK

To determine the histologic changes produced by toxic, foreign protein, and anaphylactic shock the brains of many human beings who had died of infections and of eclampsia have been examined; and laboratory studies have been made of the brains, livers, and adrenals of many animals into which had been injected toxins of streptococci, staphylococci, colon bacilli, gonococci, and tetanus bacilli; of animals to which had been given intravenously placental extract, peptones, leucin, skatol, extract of feces, alien blood-serum; and of animals in anaphylactic shock. Without exception the cells of the brain, the liver, and the adrenals showed precisely the same changes as were seen under traumatic injury and under emotional injury, first a stage of *hyperchromatism*, followed by a stage of *chromatolysis*, and—in a small percentage—a final stage of disintegration. Of special interest is the fact that these various toxins and foreign proteins as well as anaphylaxis and placental extract produced a large increase in adrenalin output (Figs. 15–18). These agents, however, caused no increased output of adrenalin under the following conditions: if the nerve-supply of the adrenals had first been divided or if the blood-vessels supplying the adrenals had first been clamped.

DRUGS—ANESTHETICS, NARCOTICS, AND STIMULANTS

Many histologic examinations of the brain cells and observations of the adrenalin output by Cannon's method were made after the administration of ether, urethane, nitrous oxid, and morphin. None of these caused either brain-cell changes or increased the output of adrenalin except in the case of ether during the stage of excitement.

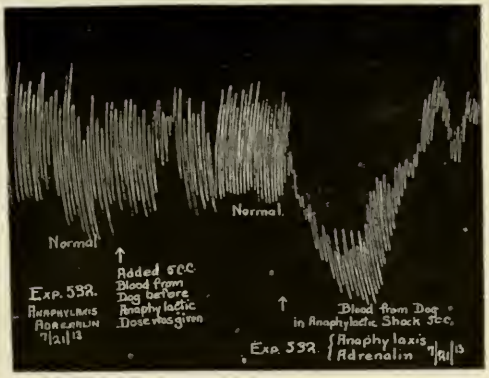
Here again it is of especial significance to note that under heavy morphin dosage there was no notable change in the cells of the brain, the liver, and the adrenals, and no increased output

of adrenalin as a result of anaphylaxis, or of the intravenous injection of toxins or of foreign proteins (Fig. 19). It was found also that the *normal* output of adrenalin was diminished by morphin. Strychnin, on the other hand, caused cell changes of precisely the same type as did the emotions, the toxins, and foreign proteins, viz., at first *hyperchromatism* and later *chromatolysis;* and there was also increased output of adrenalin. Previous division of the adrenal nerve-supply prevented the increased output of adrenalin, whatever the form of excitation.

These experimental results may be summarized as follows: All the above-mentioned agents that caused the activation of the *kinetic system,* whether emotional excitant, toxin, foreign protein, or drug, produced identical changes in the cells of the brain, the liver, and the adrenals, and also increased the output of adrenalin. On the other hand, the anesthetics, *if given for a short period only,* and the narcotics caused neither notable brain-cell changes nor increased the output of adrenalin, while strychnin did both.

ANEMIA

The loss of blood from any cause, if it be sufficient to cause a low blood-pressure and if it be continued long enough, will cause deteriorating changes in the brain cells. In our researches on anemia and resuscitation Dolley and we found that animals which had been dead for more than six or seven minutes could not be resuscitated. The recent work of Cannon offers a probable explanation of the characteristic brain-cell changes in anemia, viz., the rapid formation of lactic acid in the muscles. Loeb has pointed out the fact that intracellular acidosis develops in the absence of oxidation. If the hemorrhage be continued long enough and the blood-pressure be low enough, some brain cells will be permanently lost; hence in cases of critical hemorrhage certain—perhaps only a few—brain cells are permanently lost.


Normal
Added 5cc. Blood from Dog before Anaphylactic Dose was given
Exp. 592. Anaphylaxis Adrenalin 7/21/13
Normal.
Blood from Dog in Anaphylactic Shock 5cc.
Exp. 592. Anaphylaxis Adrenalin 7/21/13

A

Added 5cc. Control Blood from Dog
Added 5cc Blood from Dog 5 min. after Intravenous Injection of 15 c.c. Beef Serum.
Added a few Drops Pure Adrenalin.
Exp. 563. Adrenalin - Serum - Morphia.
8/14/13 Dog.

B.

FIG. 19.—TRACING ILLUSTRATING PROTECTIVE EFFECT OF MORPHIN IN ANAPHYLACTIC SHOCK.

In A the adrenalin which appears in the blood as a result of *anaphylaxis* inhibits the contractions of the intestinal muscle. Tracing B shows that the injection into a morphinized animal of beef-serum, which in the normal animal would have caused a strong anaphylactic reaction and a greatly increased output of adrenalin, causes no increased output of adrenalin as is evidenced by the contractions of the intestinal muscle as in normal blood. Since morphin acts directly upon the brain, this experiment evidences not only the protective effect of morphin but also the dependence of the adrenal upon the brain for its activity.

It might be supposed that the brain-cell changes found in cases of surgical shock are entirely due to low blood-pressure. That a low blood-pressure is an important factor is unquestionable in the light of our brain-cell studies, but that it is not the only factor is proved by the following experiment:

The blood-vessels of two animals were anastomosed. One of the animals was then traumatized, and as its blood-pressure began to fall, fresh blood was added, so that during the entire séance of trauma the blood-pressure was maintained at or near the normal level. Specimens of the brain were removed from the animals before death and brain-cell changes were found, *but it required much more trauma to produce brain-cell changes in animals whose blood-pressure was kept at the normal level than in animals whose blood-pressure was allowed to follow its downward course unchecked.* We were able to kill animals by shock in spite of an adequate blood-pressure. Therefore anemia is only one factor in the production of shock.

THE CONCENTRATION OF BLOOD IN SHOCK

The concentration of the blood in shock was investigated in our laboratory by Drs. Hitchings, Lenhart, and Eisenbrey,[1] who found that the hemoglobin and the red cell count were increased in the acute stage of shock.

In one experiment on shock the red cell count rose from 5,920,000 to 7,200,000, an increase in the concentration of 22 per cent. The increased concentration of the blood is one of the phenomena of shock. The white cell count is not much changed. In hemorrhage the red cell count falls and the white cell count rises.

[1] G. W. Crile: Hemorrhage and Transfusion (1909), p. 75.

WHAT PART OF THE INTRACELLULAR ACIDOSIS IS DUE TO EXCESSIVE WORK OF THE BRAIN CELLS? WHAT PART IS DUE TO THE BY-PRODUCTS OF METABOLISM CARRIED TO THE BRAIN CELLS BY THE BLOOD?

If the *kinetic theory of shock* be correct, then, if the circulations of two dogs be so anastomosed that their blood-streams intermingle freely, and if only one animal be traumatized, the functional impairment and the brain-cell changes will be seen principally in the animal which receives the injury. On the other

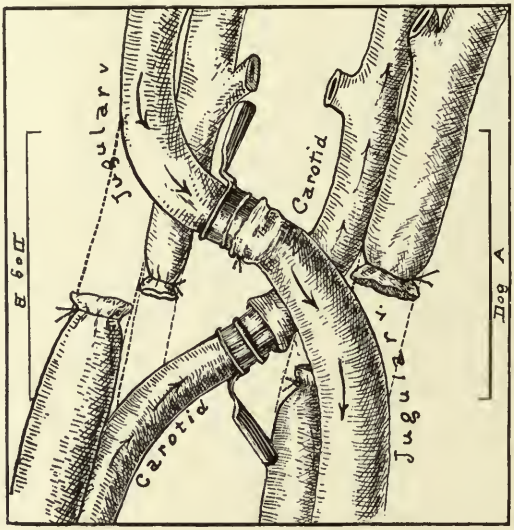
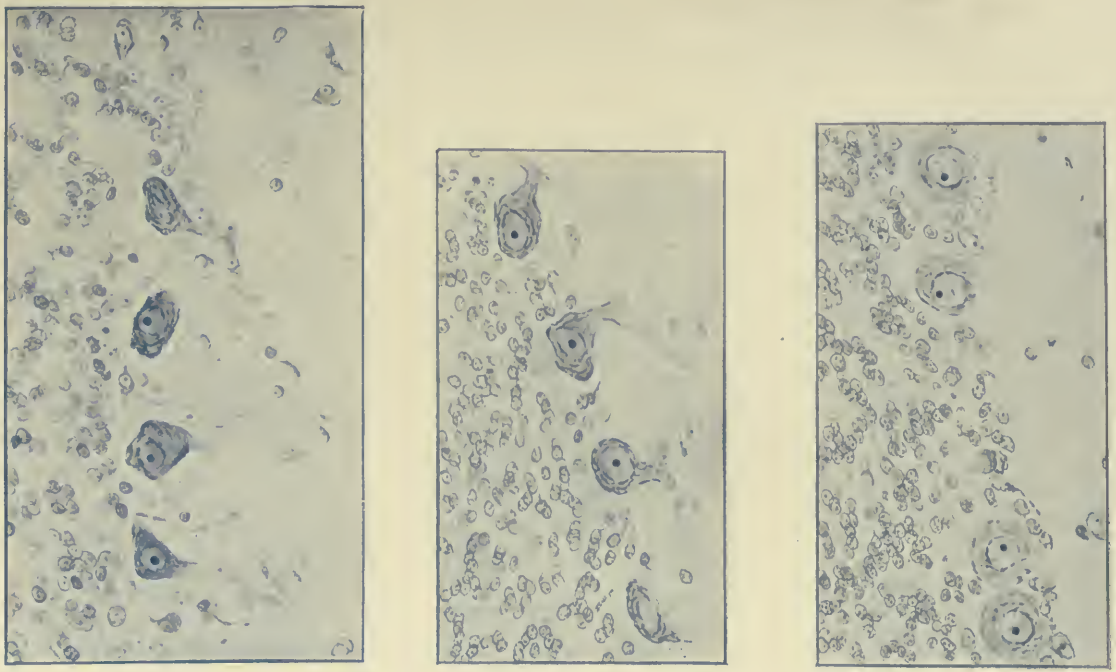


FIG. 20.—SYMBIOTIC SHOCK. DIAGRAM SHOWING ANASTOMOSIS OF THE CIRCULATION OF THE TWO DOGS.

hand, if shock be due to the altered composition of the blood whereby the brain cells are affected secondarily, then both dogs will suffer equally and the brain cells of both will show like signs of deterioration. To test this crucial point the following experiment was performed:

The proximal end of one carotid artery of Dog A was anastomosed with the distal end of the corresponding carotid artery of Dog B (Fig. 20), and one jugular vein of Dog A was then anas-



A B C

FIG. 21.—SYMBIOTIC SHOCK. THE COMPARATIVE EFFECTS OF TRAUMA ON THE BRAIN CELLS OF THE UNTRAUMATIZED DOG (B) AND OF THE TRAUMATIZED DOG (C).

A, Section from cerebellum of normal dog. B, Section from cerebellum of Dog B in symbiotic shock experiment. C, Section from cerebellum of Dog A in symbiotic shock experiment.

tomosed with the corresponding vein of Dog B, so that the blood-streams of both animals intermingled with entire freedom and in large volume. The dogs were approximately of equal weight and like physical condition. For two hours Dog A was traumatized. The animals were killed simultaneously, and their brain cells were studied by parallel technic. The examination showed brain-cell changes—typical exhaustion changes—most marked in Dog A, the dog whose body had been traumatized, and no brain-cell changes in Dog B (Fig. 21) whose body had not been traumatized, but through whose brain the blood of the traumatized dog flowed freely during the two hours. This result supports the *kinetic theory*, and opposes any theory which implies that gaseous changes in the blood or the presence of toxic products from traumatized muscles are the only cause of the brain-cell changes, though gaseous changes and toxic products may be undoubtedly important factors.

ACIDOSIS AND SHOCK

Acute blood acidosis and diminished reserve alkalinity are seen in shock. Were the cause of exhaustion limited to changes in the blood, then alkalinization of the blood would be expected to cure; but alkalinization of the blood, though it may improve the condition, does not cure exhaustion either in the clinic or in the laboratory.

(*a*) *Positive Laboratory Findings.*—In our laboratory in experiments conducted in 1912, 1913, and 1914, in collaboration with Dr. M. L. Menten, in which the gas chain method with Michaelis' apparatus was used, we found that the H-ion concentration (or acidosis) of the blood was increased:

1. During inhalation anesthesia.
2. During intense fear in rabbits.
3. During intense rage in cats.
4. During intense exertion in various animals.

5. In surgical shock.
6. In alcoholic intoxication.
7. In hemorrhage.
8. In asphyxia.
9. Several hours after excision of the liver.
10. Near the death-point after excision of the adrenals.
11. Near the point of dissolution, whatever the cause of death.

Of special interest was the fact that we found *increased H-ion concentration in overwhelming excessive energy-transforming activities.* Apparently the corrective mechanism could not dispose of the increased acid by-products as fast as they were produced. We found increased H-ion concentration as a result of *interference* with the corrective mechanism, as well as in cases in which the corrective mechanism was overwhelmed.

(*b*) *Negative Laboratory Findings.*—We found, further, that the H-ion concentration was not increased in:

1. Narcosis—by opium and its derivatives.
2. During sleep.
3. During protracted consciousness unbroken by sleep until near the death-point.
4. After decapitation in animals in which artificial respiration was maintained.
5. In *many instances* of serious, even fatal diseases, such as infections, exophthalmic goiter, cardiovascular disease, typhoid fever.

Morphin in Relation to Increased H-ion Concentration.—We found that if morphin in large doses was given during increased H-ion concentration of the blood (acute acidosis), such as is present in intense rage, intense muscular exertion, or under inhalation anesthesia, the correction of the state of acidosis was interfered with, even prevented. For example, a vigorous male cat in which induced rage and struggle brought on a markedly increased H-ion concentration of the blood was given heavy doses of morphin; the

animal remained in acute acidosis for three and a half hours and died in acidosis. In other experiments equally large doses of morphin interfered with the overcoming of the acidosis of inhalation anesthesia. The ill effects of morphin in certain types of cyanosed patients are well known to clinicians. *The soldier who is exhausted and cyanosed should, therefore, not have morphin. After cyanosis disappears* morphin is most useful.

Disappointed in the value of observations on the H-ion concentration of the blood, we tested the value of observations on reserve alkalinity.

Reserve Alkalinity and Acid Excretion in the Urine.—When the Van Slyke method for determining the reserve alkalinity of the blood was published it seemed that this, at last, would give a true indication of the reserve vitality of the patient. Through the collaboration of Drs. W. J. Crozier and W. B. Rogers this method was investigated as to its availability in the clinic, to determine the surgical risk. Drs. Crozier and Rogers in 1915, and until April, 1917, Drs. Rogers, Harrison, and Mosiman made numerous observations on the reserve alkalinity of the blood (Van Slyke method), and in the laboratory and the clinic repeated the work of Professor Henderson on the acid excretion in the urine. Their findings may be summarized as follows: Laboratory animals in shock, under anesthesia, in infection, in asphyxia, in strychnin-poisoning, in hemorrhage, in iodoform-poisoning, in exertion, in emotion showed varying degrees of reduction in reserve alkalinity, and alterations in the acid excretion in the urine. *The method played more true when an acute overwhelming drive with which the corrective mechanism could not keep pace was made than in other instances.* When time for compensation had elapsed the reserve alkalinity afforded less accurate information.

It was in the clinic that our best estimation of the value of reserve alkalinity and acid excretion determinations were ob-

tained. Here—in acute infections, in late cancers, in desperate cases of exophthalmic goiter, in good and in bad risks of all kinds —we found great and unexpected irregularity in the results. In cases of impending death, not in the stage of dissolution, but inoperable, and in cases of infection with grave prognosis that died later, the reserve alkalinity sometimes was found to be as high as in the observer, and the quantity of acid excretion of urine was not materially disturbed.

Therefore, after five years of observations in the laboratory and in the clinic on the various phases of acidosis, we have reached the reluctant conclusion that these methods, despite their scientific interest, as yet offer meager clinical value.

Intracellular Problems.—Since the acid-alkali balance of the cell is attained only during the normal supply of water and food, the rhythmic alteration of consciousness and sleep, and normal oxidation, it is obvious that the solution of the problem presented by intracellular acidosis is not as simple as the correction of the acidity of a fluid in a test-tube by adding alkalies; but there must be supplied to the cell not only the means of ridding itself of its excessive acids but also the means whereby it can maintain a normally balanced oxidation. We must, therefore, get rid of the acid and establish the conditions required for continued oxidation within limits onsistent with the life of the cell. The success of the restorative measures which we shall describe lends support to these conceptions of the fundamental condition present in exhaustion, but does not explain its ultimate cause. A complete explanation of the ultimate cause must await the complete explanation of life.

Comparison of Laboratory with Clinical Observations.—*Laboratory Observations.*—As a result of our laboratory and clinical studies we are at last forced to admit that no laboratory conclusion should be considered valid until it has been tested in the

crucible of the clinic. For example, our laboratory studies of the H-ion concentration of the blood, the carbon dioxid tension, the reserve alkalinity, the acid excretion in the urine, furnished no criterion always reliable as an indication of the patient's condition.

Why should laboratory methods be less accurate than the clinical signs? Let us view this phase of the problem from a biologic standpoint.

Alkalinity and Acidity in Relation to Animal Life.—The origin of life was probably in the sea. The sea is alkaline. Animal life is continued only in an alkaline medium. When the blood becomes acid, life ends. As transformers of energy animals are constantly producing acid by-products. The acid by-products are increased in proportion to the rate of energy transformation, *e. g.*, are increased in muscular exertion, emotion, fever, etc. Therefore the organism is in constant danger of killing itself. Many animals and men have killed themselves by the excessive production of acid by-products in great muscular struggles which overcame the factors of safety, or the corrective mechanism, namely, the lungs, the liver, and the buffer substances—the reserve alkalies immediately available. It would be expected that during the vast selective struggle of animals there would have developed wide factors of safety in these corrective mechanisms against the acute acidosis of muscular, emotional, and fever crises. Not only wide margins of safety for immediate protection but also reserves of bases and alkalies in the fluids and tissues of the body, that are not available for a quick emergency, but are more gradually drawn out in prolonged crises—prolonged struggles, prolonged defenses, prolonged want of food and water, prolonged exertion, prolonged fever, etc.

Our experiments on the H-ion concentration of the blood supported this biologic conception, because we were able to overcome the factor of safety only by an intensive drive—intense mus-

cular struggle, intense emotion, etc., while after the termination of the intensive drive the normal H-ion concentration was quickly re-established, although the animal clinically was fatigued. Therefore the H-ion concentration of the blood showed only the extent to which the corrective mechanism had failed, and did not inform us to what extent the reserves had been called out or how wide was the remaining margin of safety.

The Reserve Alkalinity of the Blood.—The estimation of the reserve alkalinity told us what the reserves were in the blood at the particular time the observation was made. It gave no intimation as to the amount of reserves lying in store outside the blood—in the body fluids, in the cells, in the bones. This was left to conjecture.

An attempt to secure information by these methods is comparable to an attempt to estimate the wealth of a man by holding him up in the street and counting the ready money in his pockets (H-ion concentration), and from this count attempting to estimate his available cash reserve in the bank (reserve alkalinity); and in turn estimating his ultimate financial resources from the amount of his bank balance without taking into consideration the securities he might hold in his strong box (ultimate reserves). A man may be financially embarrassed if his immediate cash is expended; he is not bankrupt until his ultimate reserves are exhausted.

The scientific methods so far devised tell us what factors of safety are impaired in the blood at the moment the observations are made, but do not inform us of the extent of the reserves. Our present laboratory methods do not tell the whole truth as to the actual state of the patient.

Clinical Observations.—What of the clinical phenomena? Here we have a method of greater accuracy for estimating the reserves. The respiratory center is governed by the H-ion con-

centration of the blood and has been evolved to respond with infinite accuracy to acidosis. It consists of nerve-cells and fibers, and these cells, like other cells of the body, are modified by every passing phase of chemical change in the blood. In the respiratory center we have a mechanism of surpassing delicacy and accuracy which not only reacts to intracellular acidosis but also has been evolved through eons to fulfil that purpose so correctly as to preserve life and health. Moreover, this delicate *living mechanism* is placed in the seat of life itself, while the *man-made laboratory mechanisms* are not only clumsy, but are outsiders.

This center responds to every phase of acidosis—the acidosis of asphyxia, of hemorrhage, of emotion, of exertion, of acid injection, of anesthesia, of injury—the entire gamut. It not only responds accurately, but its response is dramatically staged, so that not only the trained professional eye, but the bystander, even the patient himself, cannot escape its obtrusive evidence of increased activity.

The nerve-cells of the respiratory center, however, are not only nerve-cells that are modified by acidosis; the cells that fabricate muscular and mental action are modified also; *their power to do work is diminished.* If their activity were increased to the same extent as the activity of the nerve-cells in the respiratory center is increased, then the amount of muscular work done and the consequent amount of acid by-products would be increased, resulting in certain disaster; but the nerve-cells that drive the muscles and express the emotions are impaired. Hence we have *increased* respiratory action and *diminished* muscular action—*a corrective antithesis.*

THE INFLUENCE OF THE INHALATION ANESTHETICS UPON SHOCK PRODUCTION

In accordance with our theory that the morphologic changes in the brain cells are produced by the alterations in their internal

respiration which involve oxidation, one would expect to find that a given amount of trauma under an anesthetic like nitrous oxid, which interferes with the use of oxygen, would produce less change than an equal amount of trauma in an animal under ether; for ether, as compared with nitrous oxid, owes less of its anesthetic property to its interference with the use of oxygen by the brain cells. Testing this point experimentally, we found that under approximately equal trauma the changes in the brain cells were

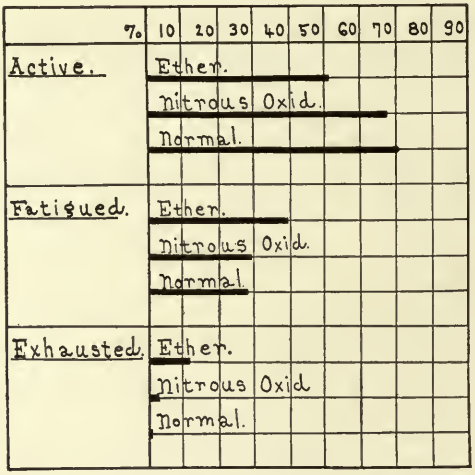
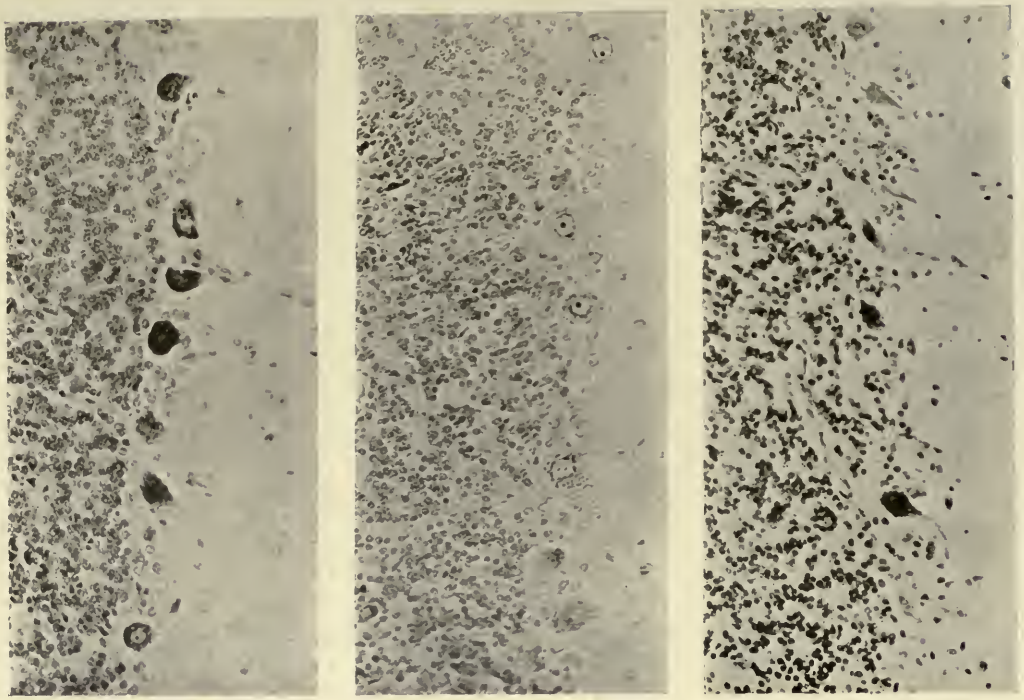


FIG. 22.—DIFFERENTIAL PURKINJE CELL COUNTS, SHOWING COMPARISON OF THE EFFECTS OF SHOCK UNDER ETHER ANESTHESIA AND UNDER NITROUS OXID-OXYGEN ANESTHESIA.

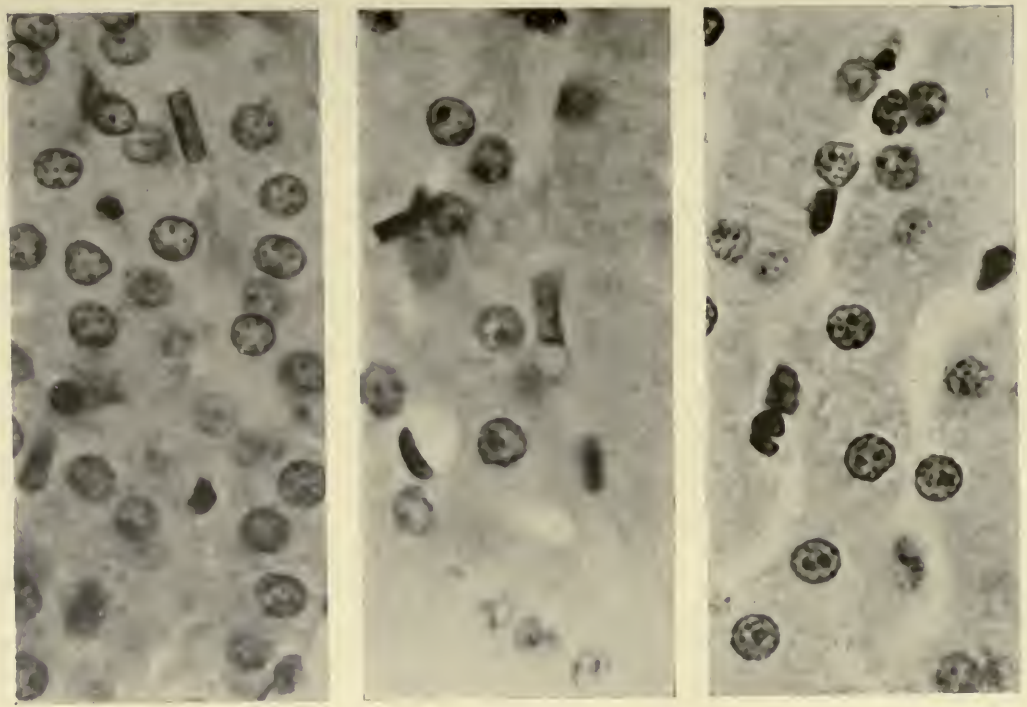
approximately three times as great under ether anesthesia as under nitrous oxid-oxygen anesthesia (Figs. 22–25); that the fall in the blood-pressure was on the average two and one-half times greater under ether than under nitrous oxid-oxygen; and finally, that the condition of the animal was worse after trauma under ether than after equal trauma under nitrous oxid-oxygen. In the course of surgical operations one observes constantly the protective effect of nitrous oxid-oxygen anesthesia. This may be



A B C

FIG. 23.—COMPARISON OF THE EFFECTS OF ETHER AND OF NITROUS OXID ON THE BRAIN CELLS OF DOGS.
(From photomicrographs × 310.)

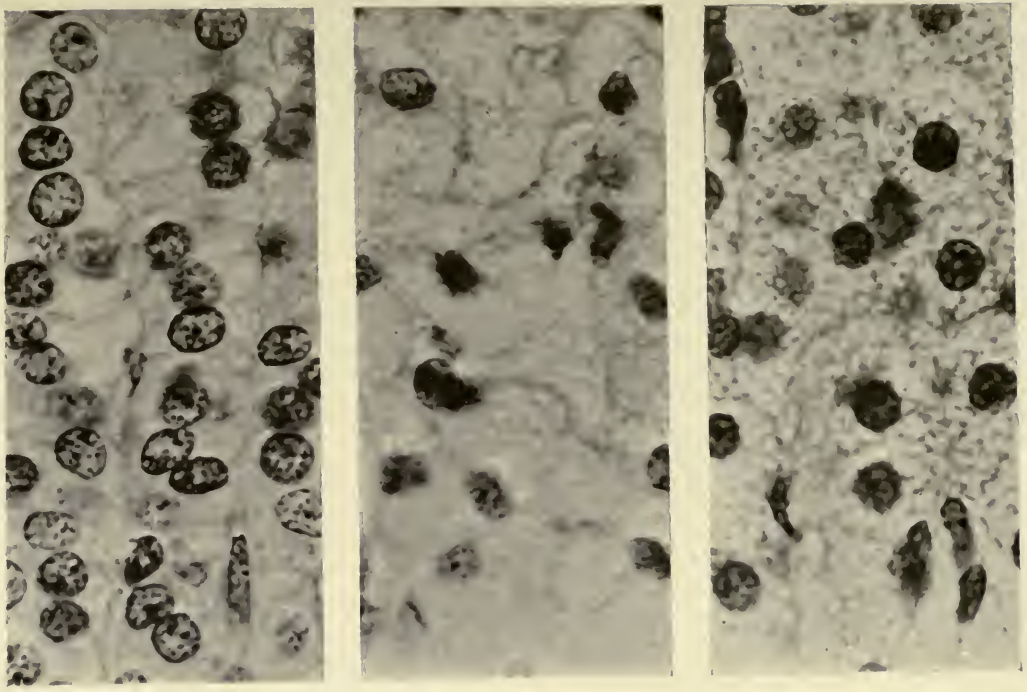
A, Section from normal cerebellum of a dog. B, Section from cerebellum of a dog after the continuous administration of ether for four hours. C, Section from cerebellum of a dog after the continuous administration of nitrous oxid for four hours.



A B C

FIG. 24.—COMPARISON OF THE EFFECTS OF ETHER AND OF NITROUS OXID ON THE LIVER OF DOGS.
(From photomicrographs × 1640.)

A, Section from normal liver of a dog. B, Section from liver of a dog after the continuous administration of ether for four hours. C, Section from liver of a dog after the continuous administration of nitrous oxid for four hours.



A B C

FIG. 25.—COMPARISON OF THE EFFECTS OF ETHER AND OF NITROUS OXID ON THE ADRENALS OF DOGS.
(From photomicrographs × 1640.)

A, Section from normal adrenal of a dog. B, Section from adrenal of a dog after the continuous administration of ether for four hours. C, Section from adrenal of a dog after the continuous administration of nitrous oxid for four hours.

regarded as in harmony with the *kinetic theory of shock* (Fig. 26).

Cannon has observed that the reserve alkalinity of the blood is better sustained during operations under nitrous oxid-oxygen than in operations under ether.

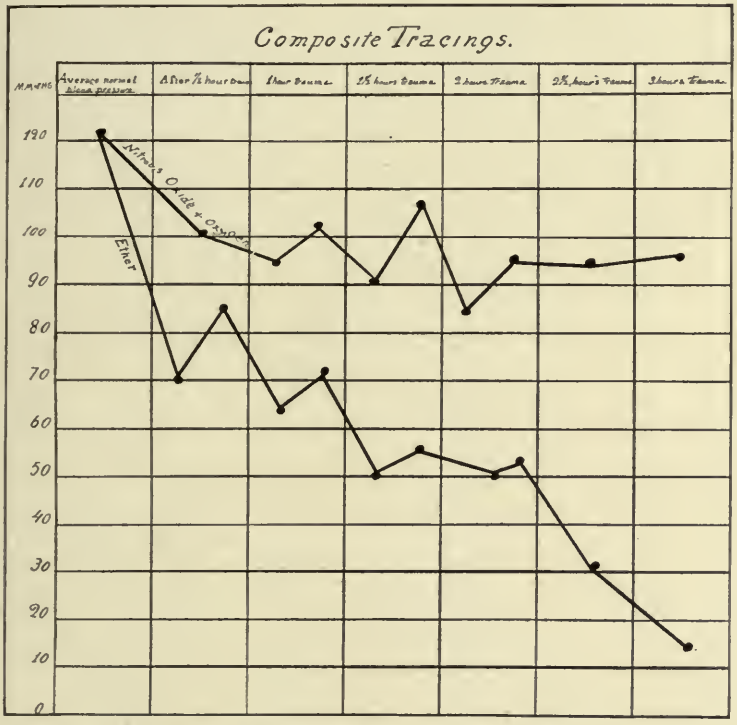


FIG. 26.—CHART COMPILED FROM LABORATORY EXPERIMENTS ILLUSTRATING THE PROTECTIVE EFFECT OF NITROUS OXID-OXYGEN ANESTHESIA IN CASES OF SHOCK, AS EVIDENCED BY THE MAINTENANCE OF THE BLOOD-PRESSURE.

Gregory Marshall, a physiologist and an expert anesthetist, after an extensive investigation of the effects of anesthetics in military surgery, concluded that in operations performed under ether anesthesia the blood-pressure was sufficiently maintained during the operation, but fell later; while in operations under

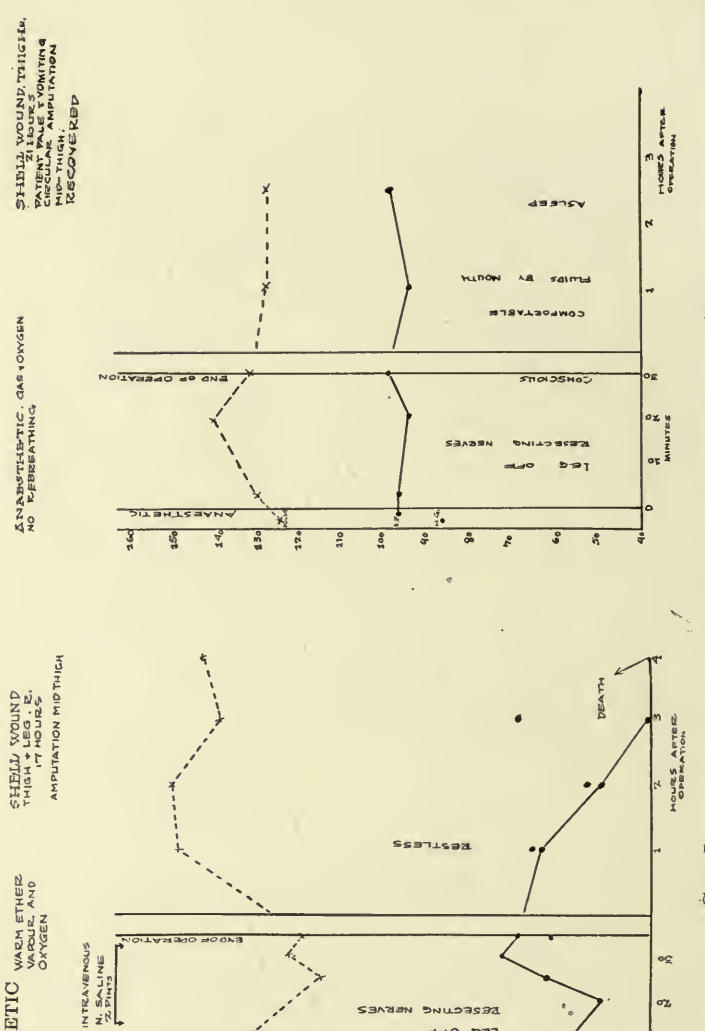


FIG. 27.—COMPARATIVE EFFECTS OF ETHER AND OF NITROUS OXID IN WAR SURGERY.
(By courtesy of Captain Gregory Marshall.)

In each of the cases here charted the thigh was shattered by a shell, necessitating a mid-thigh amputation. Compare the rapid decline to death of Case I (ether) with the postoperative course to recovery of Case II (nitrous oxid).

nitrous oxid-oxygen the blood-pressure was sustained not only during but also after the operation (Figs. 27, 28).

The mere excitation due to the feeling of suffocation while inhaling ether causes a certain amount of exhaustion from which

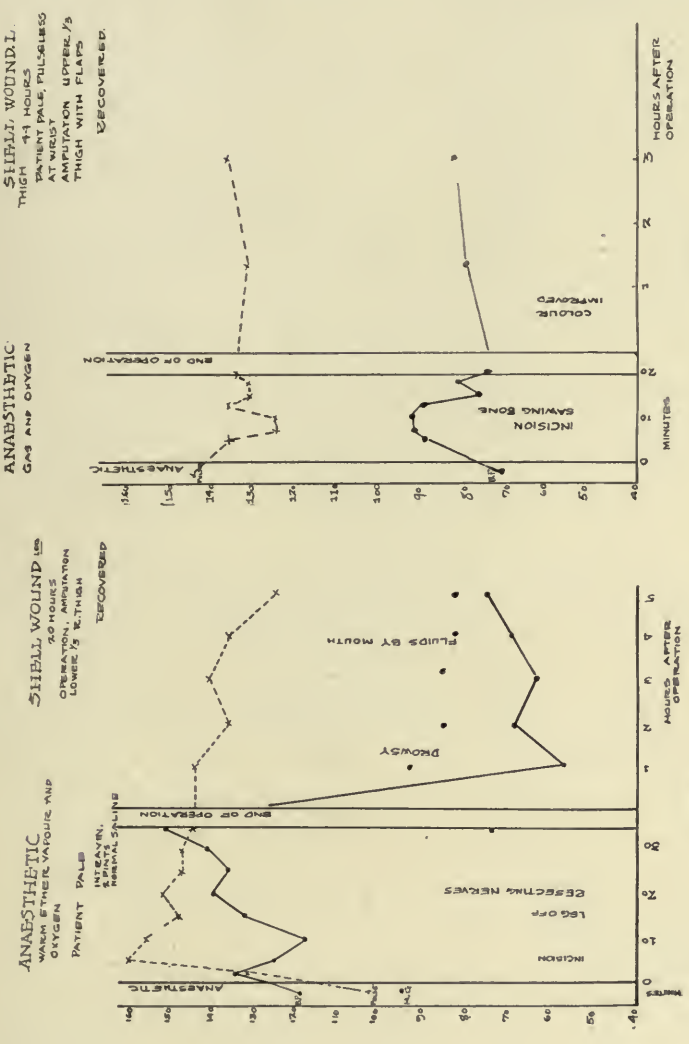


FIG. 28.—COMPARATIVE EFFECTS OF ETHER AND OF NITROUS OXID IN WAR SURGERY.
(By courtesy of Captain Gregory Marshall.)

As in Fig. 28, in each case the thigh was shattered by a shell, necessitating amputation. Compare the stormy postoperative course of Case I (ether) with the postoperative course of Case II (nitrous oxid).

the patient taking nitrous oxid-oxygen is spared. Moreover, prolonged deep ether anesthesia alone causes prolonged exhaus-

tion with marked changes in the cells of the brain, the liver, and the adrenals. This exhaustion may continue even for twenty-four hours after prolonged deep ether anesthesia.

We may conclude, therefore, that while the brain-cell changes resulting from a surgical operation are not markedly due to the inhalation anesthetic *per se*, yet their extent is to a considerable degree determined by the anesthetic which is used. As these changes are less marked under nitrous oxid-oxygen than under ether, the former should be the inhalation anesthetic of choice. In any and all cases the patient should not be permitted to be cyanotic—cyanosis indicates acidosis.

HOW DOES TRAUMA UNDER ANESTHESIA CAUSE SHOCK?

The clinical clue to the cause of shock in a surgical operation under inhalation anesthesia was given by the observation of the behavior of animals under deep and under light anesthesia during the infliction of physical injury. Under surgical anesthesia rough handling of the tissues is usually accompanied by a marked increase in the respiratory rate and by alteration of the blood-pressure.

Muscular response to trauma under inhalation anesthesia may be only purposeless moving, but when the anesthesia is sufficiently light and the trauma is sufficiently severe, movements—unmistakably purposive—are produced. To injury under inhalation anesthesia every grade of response may be seen, varying from the slightest change in respiration or in blood-pressure to a vigorous defensive struggle. As to the purpose of these subconscious movements there can be no doubt—*they are efforts to escape from injury*. The respiratory centers and the circulatory centers are doing their part by crying out—by trying to effect escape. So, too, we may suppose that all the rest of the brain cells are doing their part by stimulating the motor mechanism for defense or

FIG. 29.—ATHLETE. NOTE THE ACTIVATION OF HIS MOTOR MECHANISM AS PORTRAYED IN HIS FACIAL EXPRESSION.

escape, but, because of the anesthetic paralysis, the voluntary muscles cannot express themselves. Were it not for the muscular paralysis the patient's face, without doubt, would express motor activity as strongly as it is expressed in the accompanying picture of the athlete whose motor mechanism is driven by voluntary impulses only (Fig. 29). *The units of the motor mechanism of a patient under inhalation anesthesia may be driven even more powerfully, though in silence, throughout the course of a surgical operation.*

The result is the same as it would be if a major surgical operation were to be performed under curare alone. Curare completely paralyzes all voluntary muscles, but produces no anesthesia. It therefore gives complete muscular relaxation—a dead paralysis that would satisfy the roughest surgeon. During such an operation there would be absolute stillness, but after the paralyzing effect of the curare had worn off and the patient had again become able to express himself, what would he say? What would the surgeon think? Yet the surgeon daily inflicts equally great injury upon the brain of the anesthetized patient. For this reason a patient who enters the operating-room in the flood of health and with composed face may emerge broken and shattered and with the facies of the tortured from a severe, perhaps rough, operation under inhalation anesthesia.

COMPARATIVE SHOCK-PRODUCING EFFECTS OF TRAUMATA OF DIFFERENT PARTS OF THE BODY

It is significant that the facility with which shock may be produced depends upon the part of the body injured and upon the type of trauma to which the part is subjected. We have stated that shock is the result of brain-cell exhaustion caused by powerful or frequently repeated stimuli received through the nerve ceptors. We should then expect that the greatest brain-cell exhaustion and consequent shock would result from injuries to those

parts of the body most richly supplied with sensory nerves—*i. e.*, nociceptors.

We have stated also that the nociceptors are most abundant in those parts of the body which, in the course of evolution, have most frequently been subjected to injuring contacts with environment; that is, the nociceptors are a part of the mechanism for self-defense which during the ages of evolution has been gradually developed for the preservation of the individual and, consequently, of the species.

On this basis the hands and feet and the trunk should have many nociceptors; while the brain, which through probably the greater part of man's evolution has been protected by a skull, should have none. The first premise needs no experimental proof—daily experience is sufficient to prove to every one the rich endowment of the exposed portions of the body with these warning nerve-endings. As to the second premise—it is known clinically that even in conscious patients explorations for brain tumors with a probe elicit neither pain nor any evidence of altered physiologic functions. Realizing, however, the importance of conclusive proof of the fact that the brain possesses no nociceptors, a series of careful experiments were made. The cerebral hemispheres of dogs were exposed by the removal of the skull and dura under ether and local anesthesia. Then in each animal one entire hemisphere was slowly but completely destroyed either by rubbing it with a piece of gauze or by burning. In no instance was there more than a slight response of the centers governing the circulation and respiration, and *no morphologic change was noted in the brain cells of the uninjured hemispheres.* Collapse from interference with the medullary centers is not, of course, true surgical shock.

We must conclude, therefore, that the brain contains no mechanism—no nociceptors—the direct stimulation of which causes

activation of the brain cells. That is, direct injury of the brain can cause no purposeful nerve-muscular action, while direct injury of the hand, for example, does cause purposeful nerve-muscular action. In like manner the deeper portion of the spinal region, the lungs, and the parts protected within the thoracic cavity, have been sheltered from trauma, and they show but little power of causing a discharge of nervous energy in response to injury. Since, in the harsh period of man's evolution, injury to the heart, the brain, and the lungs led to immediate fatal results, there was no opportunity through natural selection for the development of a protective muscular reaction. These parts of necessity, therefore, were placed under special structural protection. On the other hand, injuries of the abdomen and of the chest expose larger areas to the air and cause intense discharges of nervous energy, these regions standing first in their capability for shock production.

Next in order follow the extremities, the neck, and the back. In the extremities the sole and the palm are more susceptible to shock-producing injury than are the dorsa; within the abdomen the region of the diaphragm is more susceptible than that of the pelvis; the kidneys, the ureters, and the urinary bladder have a relatively low shock-producing value, while the omentum is practically a negative tissue. As one would expect, however, injuries to the peripheral nerve trunks produce intense shock. As to the abdomen, it is probable that the great facility with which shock is produced by rough manipulations within the abdominal area may in part be due to the mechanical interference with the flow of blood in the great veins, and in part to other causes not as yet clearly apparent.

COMPARATIVE SHOCK-PRODUCING EFFECTS OF DIFFERENT TYPES OF CONTACT AND TRAUMA

Not only is the degree of shock dependent upon the *part* of the body injured, but it varies also with the *type* of trauma inflicted. Powerful response is made to crushing injuries by environmental forces; to such injuring contacts as resemble the impacts of fighting; to such tearing injuries as resemble those made by teeth and claws. That is, injuries which resemble those inflicted by physical environment or by the carnivora in fighting each other and in killing their prey are the most efficient shock-producing traumata that are known.

As a significant corollary to these observations we must note that there is no nerve-muscular response—and consequently no shock—as a result of injuries inflicted by forces which are of such late development that they played no part in evolutionary history. For example, heat is a stimulus which has existed since the days of prehistoric man, while the *x*-ray is a discovery of today. Every one knows the intense shock produced by burns with fire, while the *x*-ray may injure the bodily tissues, even to their destruction, without producing shock. There was no weapon in the prehistoric ages which could move at the speed of a bullet from a modern rifle; therefore, while slow penetration of the tissues produces great pain and muscular response, with consequent exhaustion, there is slight, if any, response to the swiftly moving bullet. The only obvious defense against such injury is strategy. For the same reason the sharp division of tissues by cutting produces less response than blunt injury. *Indeed, one might imagine that the body could be cut to pieces by a superlatively sharp knife applied at lightning speed without material nerve-muscular response—hence, without shock.*

From this phylogenetic premise we should also conclude that there are no nociceptors for heat within the abdomen, because

during countless years of evolution the intra-abdominal region never came into contact with heat. That this inference is correct is shown by the fact that the application of a thermocautery to the intestines when completing a colostomy in a conscious patient produces absolutely no pain.

On the other hand, just as the outer portions of the body—the skin, the ear, the nose, the sole of the foot, etc.—have developed the specific types of nociceptors best adapted for their specific protective purposes, so the abdominal viscera have developed equally specific nociceptors as a protection against nocuous influences. We must believe that there has always been the danger of perforations from ulcers in the gastro-intestinal tract, of infections following tearing injuries from without; of appendicitis, of gall-stones, of peritonitis from various causes, and of overdistention of the hollow viscera from various forms of obstruction. So we find that while the division of the intestines with a sharp knife causes no pain and consequently no nerve-muscular response, pulling on the mesentery does elicit pain and protective response because such pulling *resembles the pulling of distention.* Ligation of the stump of the appendix causes sharp, cramplike pain; distention of the gall-bladder and of the intestines causes pain; and all these conditions may be accompanied by prostration and exhaustion.

In the course of abdominal operations rough manipulation of the parietal peritoneum often causes a marked increase in the respiratory rate, especially in the expiratory force. Under light anesthesia severe manipulation of the peritoneum often causes such vigorous contractions of the abdominal muscles that the operator is greatly hindered in his work.

As to the reason for these subconscious movements, there can be no doubt—they are efforts to escape from injury. Pain, wherever or however produced, or manipulations and injuries,

which, in a conscious person, would cause pain, are invariably a stimulation to motor activity, whose ultimate object is protection. Thus by the muscular action resulting from pain we are protected against heat and cold; against too intense light; against local anemia caused by prolonged pressure upon any portion of the body. So, too, pain of greater or less intensity compels the required emptying of the pregnant uterus, and the evacuation of the intestine and of the urinary bladder.

SPECIFICITY OF NERVE-MUSCULAR RESPONSE TO ADEQUATE STIMULATION LEADING TO EXHAUSTION

We find that the distribution of pain ceptors corresponds to the areas of most frequent physiologic and pathologic injury, their function being the production of some kind of advantageous muscular action. Pain and muscular action are closely related. The kind of operative technic that would cause the greatest pain in the absence of anesthesia is the kind that causes the greatest degree of shock.

It should be noted that in every instance the muscular activity resulting from pain is specific in its type, its distribution, and its intensity. This specificity is true not only of pain which is the result of external stimulation, but is true also of the pain associated with certain types of infection. The infections which are associated with pain are those in which the bacteria may be spread by muscular action and in which the fixation of parts by continued muscular rigidity is an advantage. As a striking corollary to this fact we find that the type of infection which may cause muscular action when it attacks one region of the body causes no such action when it attacks another region. On the contrary, in the case of the painless exanthemata the protective response is not motor, but chemical; that is, in the case of the painless infections the defense is by the formation of immune bodies in the

blood. In the case of the painful pyogenic infections the defense is phagocytic. In these cases the parts of the body not invaded must be protected, and this protection is secured by various forms of muscular activity. First, large quantities of lymph are poured out; second, the part is fixed by continuous contraction of the neighboring muscles; third, those muscles are inhibited which by their ordinary action would spread the infection; and wherever there is protective muscular rigidity there is also pain.

In all these infections the accompanying exhaustion—shock—is *usually* in proportion to the muscular activity excited in response to the pain stimuli. This postulate is substantiated by the brain-cell findings in persons who have died as a result of pyogenic infection and in animals which have been inoculated with various organisms. To the extent that the brain cells are damaged by infection the patient's margin of safety is reduced.

As a further proof of the hypothesis we must observe also that no muscular rigidity and, consequently, no pain is produced by pyogenic infections in those organs whose muscular contraction can in no way assist in localizing the infection. This is true of pyogenic infections in the substance of the liver; in the parenchyma of the kidney; within the brain; in the retroperitoneal space; in the lobes of the lung; in the chambers of the heart; in the blood-vessels of the chest and abdomen. The organism defends itself against the pyogenic infections by pain and muscular action for the same reason that it defends itself against physical injury by pain and muscular action. Both responses are examples of specific adaptation.

Adequate stimulation of the nociceptors for pain, however, is not the only means of causing the transformation of potential energy in the brain cells into kinetic energy. Vast amounts of energy are discharged as a result of the gentlest stimulation of the so-called ticklish areas of the body. The resultant motor activity

in such a case is a self-protective action evolved for the purpose of guarding delicate areas from contacts which might be the precursors of serious injury in most important regions of the body. The ear in man and in animals is acutely ticklish, the adequate stimulus being any foreign body, but especially an insect-like contact. The transformation of energy and consequent motor activity in horses and in cattle in response to adequate stimulation of the ticklish receptors of the ear is so extraordinary that we must conclude that in the course of evolution such activity was of great importance to the safety of the animal. A similar ticklish zone guards the nasal chambers; here the resultant activity is sufficiently powerful to dislodge and expel the foreign body causing the ticklish contact. A sudden transition from darkness to intense light is sufficient to cause sneezing. The larynx is exquisitely ticklish; the exhausting results of the coughing which may follow even slight laryngeal stimulation prove how powerful has been the consequent discharge of energy. With the ticklish areas might be classed the mouth and pharynx, which possess active receptors which respond so powerfully to the presence of noxious substances that violent motor activity is excited, as a result of which the most profound exhaustion is experienced. Other areas which are capable of discharging vast amounts of energy in response to ticklish contacts are the lateral chest walls, the abdomen, the loins, the neck, and the soles of the feet. Under present conditions the motor activity resulting from ticklish contacts with these regions is of little value to man, except perhaps the strong muscular response to even the slightest contact with the sole of the foot, which is often the means of escape from a painful injury.

Should anyone doubt the energy-producing power of the ceptors in the ticklish regions of the body, let him be bound hand and foot and then tickled for an hour. He would emerge from this test as completely exhausted as though he had experienced a rough

major surgical operation or had run a Marathon race. Another witness to the exhausting effect of stimulation of one of these sensitive regions is the testimony of travelers to the prostrating results of the infliction of the bastinado, one of the most painful punishments known.

Examples of specific reaction to adequate stimulation might be multiplied indefinitely. Enough has been said, however, to show that in the course of evolution certain portions of the body were constantly exposed to injury, and that, as a consequence, special mechanisms were evolved for their adequate defense. These mechanisms consist of nerve ceptors to receive the injurious contact; of fibers to convey the stimulus to the brain; of energy stored in the cells of the brain which, upon the receipt of an adequate stimulus, is spontaneously released to produce a protective muscular activity. The truth of this postulate being granted, it becomes evident that the sum total of brain-cell energy must be diminished by each stimulus, and it follows as a self-evident corollary that the brain-cell energy will be most greatly diminished by injuring contacts with those parts of the body most richly supplied with nociceptors. The comparative shock-producing effects of operation upon different portions of the body are thus explained with the exception of cases in which interference with important functions of such organs as the liver, the brain, the heart, or the splanchnic vessels introduces another contributing non-kinetic factor. In this explanation appears *prima facie* one key to the achievement of the shockless operation—the use in these shock-producing regions of gentle manipulations and of a technic which as far as possible differs from the rough, injuring forces, to meet which the defensive mechanism was evolved through adaptation.

SHOCK-PRODUCING EFFECT OF STIMULATION OF THE DISTANCE CEPTORS—THE EMOTIONS, ESPECIALLY FEAR

As self-preservation is the most deeply rooted instinct in all living beings, so fear is the most widely distributed of the emotions, and the most powerful in its effect upon the organism. As the injured body tries to withdraw from painful, dangerous contacts, so the perception of threatened danger causes the body to be activated for escape. So powerful has the instinct to flee from anything which endangers the safety of the individual become that even distant dangers, or the mere memory of them, may cause the phenomena associated with the activity once experienced by the individual or his ancestors when escaping from a present danger. The extreme prostrating effect produced in many people by the mere sight of blood can be explained only on this phylogenetic basis.

In rabbits frightened by dogs, but not injured and not chased, the principal clinical phenomena are rapid heart, accelerated respiration, prostration, tremors, and a rise in temperature. The dogs show similar phenomena, except that instead of the muscular relaxation seen in the rabbits, they exhibit an aggressive muscular activity. Both the dogs and the rabbits are exhausted, but the exhaustion of the rabbits is greater even though the dogs may exert themselves actively and the rabbits apparently remain physically passive.

An analysis of the phenomena of fear shows that, as far as can be determined, all the bodily functions which are of no direct assistance in the effort toward self-preservation are suspended. In a voluntary expenditure of muscular energy, as in the chase or in athletic exercises, the suspension of the other bodily functions is by no means so complete. Fear, therefore, and, above all, fear associated with trauma may completely exhaust the organism even to the point of death. Not only is this true, but fear causes

a lowering of thresholds and, therefore, to the person obsessed by fear the power of all stimuli—both physical and psychic—is augmented.

After fear, anger is probably the emotion most damaging in its effects upon the body mechanism. Man partakes of the nature of both the fighting and the fleeing animals, and consequently anger alone, or fear alone, or a combination of both may possess him. A proof of the phylogenetic origin of anger is found in the fact that though the efficiency of the hands of man has largely supplanted the use of the teeth as defensive weapons, he still sets his jaw and shows his teeth in moments of great anger.

From these premises the disastrous effects of worry are readily comprehended, for worry partakes of the nature of both fear and anger. It is a chronic state of attempting to escape from some threatening evil or of anticipatory activation to combat the cause of some disaster. This conception explains many bodily impairments and diseases; it explains the viciousness, alternating with sulkiness, the progressive weakness, even to death, shown by animals in captivity. It explains the grave digestive and metabolic disturbances resulting from prolonged financial strain or anxiety. It explains the comprehensive physical changes that are wrought by sexual love and hate. It shows how almost any factor in the environment, through phylogenetic and ontogenetic associations, may influence the functions of the bodily organs. In the uncompromising law of the survival of the fittest, by which man was evolved as a motor being, each of his organs at some time in its development served in the relentless struggle.

On this mechanistic basis the emotions may be explained as activations of the entire motor mechanism for fighting, for escaping, for copulating. The sight of an enemy stimulates in the brain those patterns formed in part by the previous experience of the *individual* with that enemy, and in part by the experience of the

race with that species of enemy—the net result of the struggle and survival of the race. As an adaptive response these many brain patterns, in turn, induce an active stimulation of the energizing glands and of the muscles which produce the complete act. Captain John Frazer and Captain Cowell have found that the blood-pressure in soldiers on duty on the active front was higher than in the reserves from the same regiment who were not in acute danger. When the soldiers returned from the trenches to rest at their billets the blood-pressure immediately returned to normal. The effect of the emotions upon the body mechanism may be compared with that produced upon the mechanism of an automobile if its engines are kept running at full speed while the machine is stationary. The whole machine will be shaken and impaired and may be even destroyed.

Since the deleterious effects of worry and fear upon the body may be the result of a lack of faith, justifiable or unjustifiable, on the part of the individual in his own ability to protect himself against real or fancied hostile environmental influences, so we see that any agency which can dispel worry or can overcome fear will stop these body-wide stimulations and inhibitions which cause lesions that are as truly physical lesions as are fractures. The striking benefits of good luck, success, and happiness; of changes of scene; of hunting or fishing; of optimistic and helpful friends, are at once explained on this hypothesis. One can also understand the sudden change from the broken body and cowed spirits of an animal in captivity to a buoyant normal condition when freed.

These facts, proved by common daily experience in the clinic and in the laboratory, show how disastrous may be the effect of the terror and anxiety natural to the patient who contemplates a surgical operation upon himself, even if all effects of the actual trauma are obviated (Fig. 30).

Every surgeon knows how much better are his results in the

case of the patient who views with unconcern the preparations for the approaching operation, than in that of the high-strung nervous patient whose terror may reach such a degree that the fear phenomena are evidenced throughout the operation by an increased pulse-rate, rapid, troubled respiration, sweating, tremors, etc.

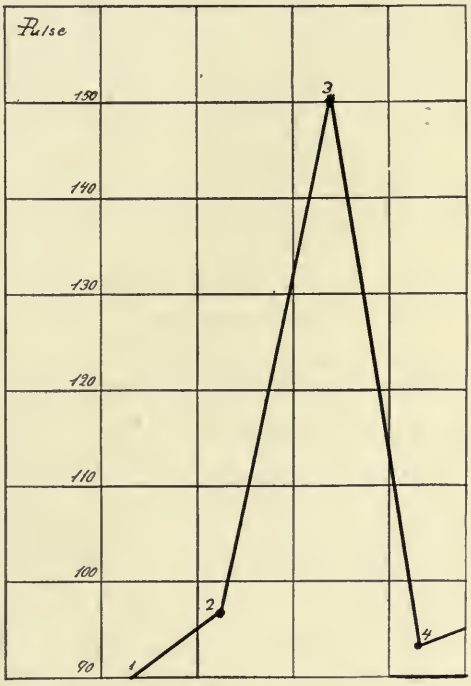


FIG. 30.—EFFECT OF STRONG EMOTION—FEAR—UPON THE PULSE.
The patient, a foreigner, was brought to the operating-room from the accident ward. Pulse and temperature normal. When he found himself in the operating-room he was greatly disturbed. It was impossible to make him understand that his leg was not to be amputated, but only a plaster cast applied. Under this psychic stimulus his pulse rose to 150, and soon he developed a temperature of 101.2° F

In addition, the patient who, prior to his operation is convinced that he will die, usually does die. The quiet, settled conviction is as potent in its effect as is the terror which holds the bird motionless as he watches the approaching serpent. The operation may

be an exploration for a suspected cancer, of the existence of which the patient feels absolutely certain. If, after the operation, he is told that no cancer was found, he is sure that the surgeon has invented a fiction for his encouragement and that an inoperable cancer actually exists. The patient has heard of such means being taken to bolster up the courage of the hopeless. If he be a physician, he may himself have been a party to such a deception. The force of this conviction will probably overbalance all the efforts of his surgeon. The overwhelming stimulus in such a case is the same as that which depresses the animal in captivity, or that which in our laboratory injured the brains of our frightened rabbits, and threw excessive amounts of adrenalin into the blood of our frightened cats; the same as that which is evident in the strain and stress of life everywhere.

In these patients without hope one sees a drawn face; the expression is despairing; digestion is arrested; and insomnia is almost unconquerable. These clinical observations are at variance with the pulse and temperature which at first are unchanged, but the hopeful chart ultimately becomes as grave as the facies, and to the astonishment of all but the experienced, death follows—a death from fear.

Internists as well as surgeons recognize that recovery is impossible or is at least prolonged in the patient who does not try to get well; and every epidemic attests the fact that many of the victims are half-killed by fear before the disease begins its easy task.

In the hospital, then, as in sports, in competition of every kind, in war, in every phase of life, faith in the outcome makes a good fighter and is half the battle. The surgeon who confines his curative measures to the operating-room has fought but half his battle, for a favorable outcome will depend not only upon his operative skill but also upon the success with which he can dispel doubts of the outcome and bolster up the confidence of his patients in their own inherent ability to meet the stress of the ordeal.

SUMMARY

The brain is the master organ, which, through the intermediation of the receptors evolved for light, heat, sound, touch, taste, smell, common sensations, as well as of the chemical receptors, directly or indirectly drives the various organs of the body. It drives the adrenals to increase the output of adrenalin; the thyroid to increase the output of thyro-iodin; the muscles to contract, etc. Adrenalin is the great oxidizer of the body. Osterhout has shown that iodin increases the electric conductivity of plants and indirectly increases metabolism. The muscles do work. The liver stores and delivers glycogen and breaks down the acid by-products of energy transformation into gases and into acid salts. Though the gaseous products are mechanically eliminated by the lungs, the acid salts by the kidney, the liver is the basic organ of acid elimination. It is obvious, therefore, that the organs that perform the basic work of energy transformation tend to run parallel courses in their relation to exhaustion and to restoration.

Whether these organs are partially exhausted, as at the end of a busy day, or completely exhausted, as in shock, their restoration is accomplished principally, perhaps only, during sleep, as far at least as is indicated by histologic findings. This gives a sound clue to our line of treatment.

The *kinetic system* is constantly activated as long as there is life, but normal activation produces fatigue, not exhaustion. If normal activity of the *kinetic system* be exemplified by walking, shock might be exemplified by the exhaustion caused by a Marathon race. The difference between normal processes and shock is one of intensity, not of kind. *From these premises it becomes obvious that the complete exclusion of both traumatic and emotional stimuli will wholly prevent the shock of surgical operations.*

CHAPTER III

THE CLINICAL PHENOMENA OF SHOCK

The outstanding phenomena of shock are:

1. Reduced metabolism.
2. Loss of body heat.
3. Loss of muscular power.
4. Loss of mental power.
5. Increased respiratory rate—increased ventilation of the lung.
6. Increased pulse-rate.
7. Lowered arterial blood-pressure.
8. Cold, moist skin.
9. Pallor—sometimes a yellowish tint.
10. Shrunken facies.
11. Cyanotic nails.
12. Dull, listless, expressionless eyes, with heavy lids.
13. Increased H-ion concentration of the blood—diminished reserve alkalinity.
14. Concentration of the blood—relatively high red blood count.

The patient in shock displays his symptoms dramatically and is self-diagnosed.

Reduced Metabolism.—Not all tissues and organs suffer a reduced metabolism in shock. The respiratory system and the circulatory system show an increased metabolism; but these organs are the minor transformers of energy; the principal energy transformation is accomplished by the massive voluntary muscular system, the brain, the liver, and other cellular tissues. Whether the total heat metabolism is increased or diminished depends on the muscular system. If the normal rate of energy transformation

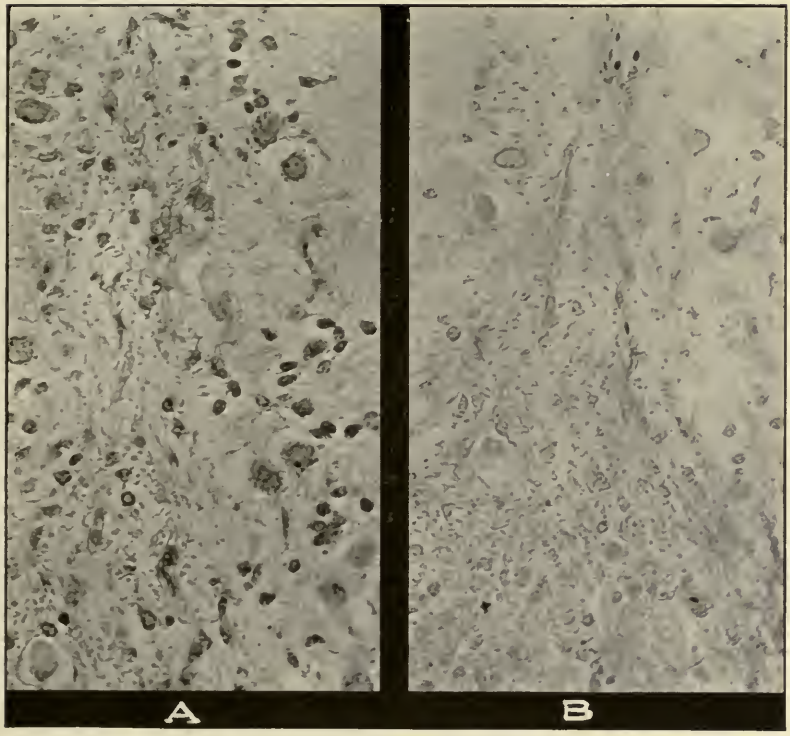


FIG. 31.—EFFECT OF THE DISCHARGE OF ITS ELECTRIC MECHANISM UPON THE CEREBELLUM OF AN ELECTRIC FISH. (From photomicrographs × 310.)

A, Section of normal cerebellum of an electric fish. B, Section of cerebellum of an electric fish after discharge. Note the general disappearance of chromatic material and the almost complete disintegration of some Purkinje cells in B.

of the massive voluntary muscular system is diminished the result will be decreased metabolism.

It must be borne in mind, as Mathews has pointed out, that it is not at all certain that the metabolism of the brain consists in the transformation of its potential energy into heat; it may convert a part—perhaps nearly all—of its energy into electricity. This would escape the calorimeter. Benedict found no increased heat production resulting from intense mental activity, yet the brain has a large blood-supply, consumes large amounts of oxygen, produces large amounts of carbon dioxid; in fact, the brain has the most active metabolism of the body, but since it apparently produces no heat it is probable that the potential energy of the brain cells is transformed into other forms of energy. The electric discharge of electric fish causes no heat, for the potential energy of its batteries is transformed into electric, not heat, energy. The result of electric discharge to the point of exhaustion on the brain cells of the electric fish is precisely the same as the change in the brain cells of man in exhaustion (Fig. 31). In our researches we have found that the electric conductivity of the brain is increased in the inceptive stage of traumatic and of toxic shock; and that it is decreased in exhaustion from any cause—trauma, emotion, exertion, prolonged consciousness (insomnia), strychnin or adrenalin injection, infection, thyroid feeding.

In curare anesthesia there is complete disconnection of the brain from the voluntary muscular system; the temperature of the body becomes that of the environment, and the animal behaves like a cold-blooded animal. Yet if an animal under curare is traumatized its brain shows typical exhaustion—typical brain-cell changes.

Loss of body heat is one of the most striking features of exhaustion. Lavoisier found that metabolism or energy transformation is increased by cold; and Sir Almroth Wright has found that acidosis is produced by cold. One would expect, therefore,

that cold would increase the degree of exhaustion just as the degree of exhaustion is increased by muscular exertion, emotion, or pain.

Increased Respiratory Rate.—In most cases of exhaustion the respiration is excessive. Some instances, however, in which the respiration is shallow seem to offer some support to the opinion of Yandell Henderson that the respiratory center needs to be stimulated by carbon dioxid.

Lowered Arterial Blood-pressure.—The arterial blood-pressure becomes lowered in every case of shock that progresses toward a grave issue. Death from surgical shock in the presence of a good blood-pressure is, we believe, unknown. Nevertheless, excessive trauma may cause the death of animals in whom a fair blood-pressure has been maintained by overtransfusion. In such cases it is probable that the progressive muscular weakness has retarded the circulation of the blood to the point of failure.

Cold, Moist Skin.—The feeble circulation and the diminished heat production account in part for the cold skin which is one of the salient features of advanced shock. The moisture is due, in part, to the fact that evaporation is retarded by the lowered body temperature, while such evaporation as does take place increases, in turn, the coldness of the body surface.

Pallor and Yellowish Tint.—The cause and the significance of pallor is obvious, but the cause of the slightly yellowish tint is not known. This yellow tint is conspicuously displayed by soldiers lying out on No Man's Land in the presence of gas bacillus infection, and in men who have been under a tremendous strain of work, worry, and loss of sleep with insufficient food and drink.

Shrunken Facies.—The characteristic shrunken facies is due, in part, to relaxation of the muscles of expression as during normal sleep; in part to the want of fluids; in part to the low blood-pressure; and possibly, in part, though if so to but a slight degree, to the imbibition of water from the blood by the acidulated tissues.

CHAPTER IV

TREATMENT OF SHOCK

EXPERIMENTAL research has shown:

1. That whatever the cause of exhaustion, restoration takes place principally during rest and sleep.

2. That rest alone, alkalies alone, hypertonic solutions alone cannot restore the normal without the aid of sleep.

3. That whatever the cause of exhaustion and the resultant cytologic lesions, sleep is the final restorer. The fact that sleep is a negative state gives a cue to one line of treatment.

The indicated treatment then consists in:

I. *Combating existing causes of exhaustion.*

II. *Establishing a state of negativity through natural sleep and through agencies that accomplish in part what is accomplished by sleep.*

I. Combating Existing Causes of Exhaustion.—The common causes of exhaustion are:

1. *Acute Anemia from Low Blood-pressure.*—One of the outstanding damaging factors in shock is the low blood-pressure. Therefore, whether or not there has been hemorrhage, if the exhaustion is so profound that life is threatened, the transfusion of blood is indicated. The principles and the technic of transfusion will be described in a later chapter. Except in chest and in head cases the foot of the bed of an exhausted patient should be elevated.

2. *Cold.*—Most exhausted patients are cold and clammy. Cold and clammy patients should obviously be warmed by (*a*) blankets; (*b*) hot air (Fig. 32); (*c*) electric-light bath. The last named treatment is preferred.

3. *Pain.*—Relieve pain by making every possible readjustment of dressings; by arranging for maximum comfort. If these means do not afford relief, and *cyanosis is not present,* give morphin.

4. *Thirst.*—If possible, give per rectum by the Murphy drip a solution of 5 per cent. glucose and 5 per cent. sodium bicarbonate. Give fluids by mouth or subcutaneously. In shock the organism is in urgent need of fluids. The natural avenues of absorption are preferable to intravenous injection.

5. *Psychic Drive.*—Overcome worry and anxiety by reassurance and attention.

6. *Acidosis.*—Secure a good exchange of fresh air. In grave crises give oxygen; push fluids and give intravenously a 5 per cent. solution of sodium bicarbonate with 5 per cent. glucose. Adrenalin is of doubtful value.

II. **Establishment of the State of Negativity.**—The most complete state of negativity and, therefore, the most potent reparative agent is sleep—*deep, untroubled sleep,* with complete physiologic rest. Sleep should be broken only for some strongly urgent reason, certainly not to substitute a less potent aid, but only to avoid a danger—to arrest hemorrhage, for example. Comfort and quiet and assurance are lesser, but strongly beneficial states, principally because they lead to sleep. The value of sleep is attested by its insistence in the intense phases of war—soldiers sleep in trenches; in mud; on stones; in rain; under bombardment; on horseback; on the march; in shell holes; on No Man's Land. They sleep with compound fractures or abdominal perforations; sleep despite pain and hunger and thirst; sleep though they may be captured; sleep on stretchers awaiting operation. In the hospital, oblivious of time, without wants, and unconditionally somnolent, the sleep-wearied soldier presents the collapsed facies that characterizes exhaustion from other causes. When at last in a comfortable bed he often sleeps for two days.

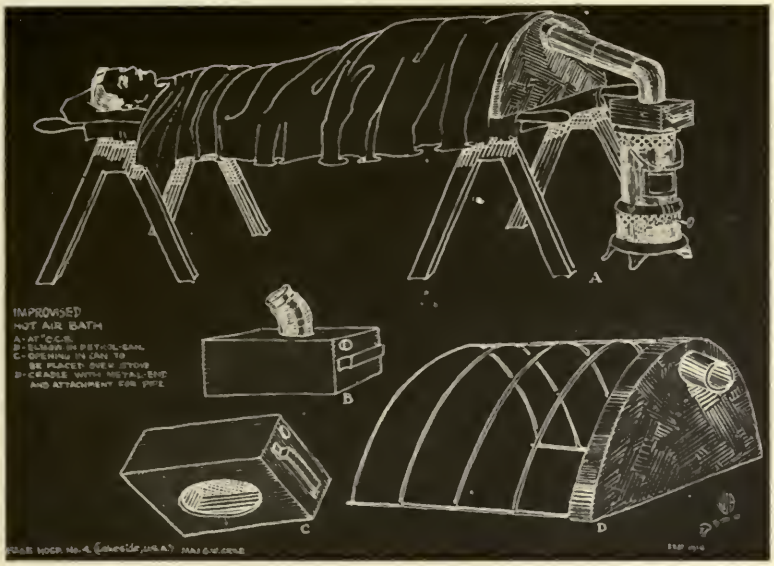


FIG. 32.—IMPROVISED HOT-AIR BATH USED AT A CASUALTY CLEARING STATION, BRITISH MEDICAL SERVICE.

When the urgent desire for sleep has been satisfied, the soldier has wants, appreciates pain, experiences hunger and thirst; the shrunken face is filled; exhaustion is relieved; normal life is restored.

The damage done by prolonged consciousness unbroken by sleep and the repair effected by sleep is demonstrated by the following summary of a research described in a preceding chapter, see pp. 37 to 49:

1. Animals become exhausted and inevitably die if kept awake continuously for from five to eight days.

2. Histologic studies of every organ and tissue of the body show constant intracellular changes in only the brain, the liver, and the adrenals. These changes are identical with the histologic changes seen in exhaustion from other causes.

3. The changed cells in these organs are restored to the normal during one period of sleep, except those brain cells whose nuclear membranes and cell membranes have been ruptured. These brain cells are not restored, but die, and are never replaced. Brain cells damaged to a degree just short of dissolution recover slowly; the remainder recover in one séance of sleep (see Figs. 4–6).

4. Substitutes for sleep.

(*a*) *Nitrous oxid-oxygen anesthesia* is a partial substitute for sleep. Given one hour in every six in an experiment continued for one hundred hours it partially protected the brain from cytologic changes, but did not accomplish as much for the liver and the adrenals. (See Figs. 23–25.) In other experiments nitrous oxid-oxygen, like sleep, partially restored the brain cells which had been damaged by other causes of exhaustion.

(*b*) *Opium* and its derivatives are partial substitutes for sleep, its protective effect being extended to all organs. If there is no cyanosis and shock is severe, establish deep opium narcosis.

From these premises we conclude that two sets of factors may influence the result of the treatment of shock—one set to be avoided, and the other to be employed.

Avoid excitement; worry; anxiety; pain; rough handling; wet; cold; stimulants, such as strychnin, camphor, mustard, alcohol. *Avoid* chloroform and ether anesthesia. *Avoid* rough operating. *Avoid large doses of morphin in the stage of deep acidosis.*

Employ comfort; solace; warmth; elevation of foot of bed; hot drinks. *Employ morphin except in the stage of deep acidosis. Employ blood transfusion. If an operation must be performed, let it be feather-edged, quick, gentle, and under nitrous oxid-oxygen, and, if practicable, local anesthesia as well.*

In grave cases give *early—not late*—blood transfusion. If the patient has been long in deep exhaustion, and presents a yellow-tinted color and is in a deep mental stupor, indicating impending final cellular dissolution, then give an intravenous infusion of 500 c.c. of a 5 per cent. solution of glucose in 5 per cent. sodium bicarbonate solution—perhaps with the addition of a few drops of adrenalin. Follow these measures by an ample transfusion of blood, as much even as 1000 c.c.; and, if indicated, operate immediately under nitrous oxid-oxygen or local anesthesia, or both combined; otherwise, under short ether or spinal anesthesia. Whatever the anesthetic, if an operation is necessary, it should be performed *deftly* and *quickly*, and with a *minimum of blood loss.*

III. **Discussion of the Physiologic Advantages and Disadvantages of Certain Protective Measures.**—*Normal Saline.*—Intravenous or subcutaneous saline infusions are useful in cases of shock of moderate severity. Their limitation is seen in the action of intravenous infusion, for if normal saline infusion be given to an animal at a slow or at a rapid rate in excessive amounts until death, two outstanding facts are noted:

(*a*) The normal blood-pressure is not raised.

(*b*) The animal dies from asphyxia due to a mechanical fixation of the abdominal muscles, the lower ribs, and the diaphragm. This fixation is caused by a vast accumulation of saline

solution in the walls and the lumina of the stomach and the intestines; *i. e.*, water runs out of the circulation through the areas through which water is normally absorbed as rapidly as it enters.

The blood cannot be more than momentarily diluted by normal saline. The value of normal saline, therefore, is hopelessly limited. Water is of great value—of most value when it is absorbed from the alimentary canal.

(*c*) The normal method of introduction, therefore, is by the stomach or through the mucous membranes by the Murphy drip. The administration of water by these routes produces no overloading, the rate of absorption is not excessive, and the results are good. Water given intravenously is rapidly eliminated from the body. Water passing through mucous membranes or absorbed from the tissues is retained and utilized to a far greater extent.

Hypertonic Solution of Sodium Bicarbonate or of Sodium Carbonate.—Will sodium bicarbonate or sodium carbonate overcome intracellular acidosis? Is the addition of glucose an advantage? Attempts to find the answer to these questions, both in the laboratory and in the clinic, have yielded the following results:

Generally speaking, sodium bicarbonate or sodium carbonate is more potent than normal saline. The blood-pressure improves more quickly and is better sustained, and the exhaustion is more relieved than by normal saline, but, nevertheless, alkalies accomplish far less than blood transfusion. Even in intracellular acidosis induced by hydrochloric acid, alkalies, such as sodium bicarbonate, cause only a temporary change in the intracellular lesion. It is only during sleep that the intracellular lesion is completely overcome. Sodium carbonate given prior to or during shock-producing trauma delays, but does not prevent, the production of shock. The addition of glucose is apparently useful.

Morphin has possibilities for good and for evil which are not yet fully appreciated. Laboratory researches have confirmed what

clinicians have experienced, viz., that morphin diminishes shock, protects against the pyogenic infections, prolongs life in precarious situations, such as shock and infection; that under morphin patients require less food, and the temperature and pulse in infections are materially controlled; that under such circumstances the morphin habit is not formed. Clinical experience shows further that morphin *does harm when patients are cyanosed.* Our researches have shown that when large doses of morphin are given to animals under deep anesthesia, or in acute cyanosed exhaustion from intense exertion, they are deprived of the power to overcome their cyanosis, *i. e.*, their acute acidosis. Therefore cyanosed patients should not receive morphin.

While morphin never causes a habit when given in these extremely critical states, it easily establishes a habit when given in cases of psychic distress, of worry, insomnia, etc. There is opportunity for wide discrimination in its use—in one case none should be given; in another case light doses may be beneficial; in other cases massive doses are most useful. When the way is clear so that massive doses of morphin may be given safely, it is a most potent agent for good.

RECAPITULATION OF THE TREATMENT OF SHOCK

1. Physiologic rest.
2. Warmth.
3. Large quantities of fluids—by mouth, by rectum, subcutaneously.
4. Elevation of the foot of the bed.
5. *In absence of cyanosis,* large doses of morphin.
6. Transfusion of blood.
7. Nitrous oxid-oxygen anesthesia.
8. Local anesthesia.
9. Quick, deft, light operation.

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CHAPTER V

ANOCIATION

On the kinetic theory already enunciated in the foregoing chapters a new principle of operative surgery has been founded. Every adequate stimulus with or without inhalation anesthesia, whether from trauma or emotion, predisposes to shock. That is to say, the sight of the operating-room, the spoken word implying danger, the taking of the anesthetic, the instrumental injury of tissues in the course of the operation, and the irritation of exposed divided nerves in the fresh wounds, together with the traction of the stitches after the operation, all are injurious stimuli. Obviously, the only practical method of protecting the brain is the development of an operative technic which will exclude from the brain the stimuli of the special senses and the stimuli of common sensation, and the employment of an anesthetic agent that does not harm, but rather acts as a protection to, the brain cells.

The principle of *anociation* may be illustrated by the wrecked *Titanic*. The story of the stress and psychic strain of the survivors is known, and that of the lost may be easily imagined; the future memory of this experience in the minds of the survivors may be safely predicted. Now, if a survivor of this ship had been so skilfully anesthetized in his bed just before the accident that he knew nothing of the impending disaster, and if he then had been carried up on deck, lowered into a life-boat, and taken aboard the rescue ship without being allowed to awaken from his anesthesia until he was safely in bed again in a comfortable state-room—if then he had been told that he had been transferred from the sinking ship, but that now he was safe and would soon see his

home—he would have passed through the stormy scene in a state of *anociation.*

Is there a single anesthetic that will exclude all nocuous or harmful physical and psychic stimuli from the brain? By blocking nerve conduction local anesthetics protect the brain from the effects of local operative injury, but *they do not protect the brain* against destructive psychic strain. Inhalation anesthetics exclude the psychic stimulation of the brain cells, but *do not exclude the operative stimulation.* Each anesthetic covers a part of the field, but there is no single agent that *alone* can produce *anociation,* which is the goal of operative surgery. We, therefore, do not advocate ether alone, chloroform alone, or nitrous oxid-oxygen alone; we do not advocate local anesthesia alone, or morphin and scopolamin alone, or spinal anesthesia alone, but through *selection* and *combination* of anesthetics we aim to secure the anesthesia that in the case in hand will exclude all stimuli from the brain, and thereby attain *anociation.*

We propose to discuss the technic by which a state of *anociation* has been attained in certain major operations; to show that by its use not only the immediate operative results but the postoperative morbidity and mortality as well are lessened or eliminated. It may be well first, however, to say a few words regarding the *anociated* environment which should be sought, since this has a scarcely less important bearing upon the outcome of the operation than has the operative technic itself.

The surgeon's best assurance for the successful outcome of a serious operation would be to have the patient come under his care long before the development of the trouble from which relief is desired. Unfortunately, this possible factor of success is not within the reach of any individual or surgeon. The surgeon, however, who too often must deal with patients heavily handicapped by factors which if known in time might have been con-

trolled, is finding that by a careful, unhastened preparation of his patient he may do much to counteract the adverse conditions.

It is apparent that the methods required to prevent shock in surgical operations must be made as automatic as walking and running, as speaking and writing; that is, we must begin with the student, continue with the intern, concentrate on the surgical resident, and so drill them and exercise them, and be examples to them, that when they are prepared to operate alone they will never need to think of the shockless technic any more than one needs to think of the movements and the inhibitions of the act of walking or of writing. Once equipped with an automatic surgical technic which includes the movements and the restraints required for the performance of a shockless operation, the attention of the surgeon may then be fully occupied with the lesion for which the operation is performed, and he will automatically avoid every factor that might cause shock.

Without question, once the habits of needlessly rough surgery have become fixed in middle life, it will be difficult to substitute other methods without interference with the required attention to the pathologic and clinical problems involved in the condition for the relief of which the operation is undertaken.

In other words, the work of the surgeon does not begin in the operating-room, nor with the immediate mechanical preparation of the patient for operation, nor does it end with the healing of the physical wound. In the operating-room and during the process of healing also the patient must be considered *as a whole.* That is, the surgeon, the members of his house staff, the hospital superintendent, the intern, the nurse, the orderly—every one who comes into relation with the patient—must bear in mind that even apparently slight factors may contribute—mightily even—to the ultimate welfare of the patient. Already we have come to realize to some extent that human beings are *integral* organisms

and that one integral part cannot suffer without the coincident suffering of most or all of the rest. Yet we are prone to forget that the reverse of the proposition must be true also—that any factor which contributes to the welfare or improvement of the condition of one essential part will contribute also to the welfare of the rest.

We have stated the importance of the emotional factor in producing shock. If the natural fear of the approaching ordeal, which is felt by every normal individual, be augmented by tactless words in a surgeon's consulting room, by an ungracious reception at the hospital, by inconsiderate treatment by a nurse or orderly, by the sound of clanking instruments, or by the rough or forced administration of an anesthetic, then the resistance of the patient, which is already depleted by his diseased condition, will be lowered still further. No matter how perfect and non-shocking in itself may be the technic of the operation, the results are still prejudiced by these other adverse factors.

By an assuring preoperative environment; by the definite dulling of the nerves through the administration of a narcotic; by a non-suffocating odorless inhalation anesthetic; by a local anesthetic to cut off all afferent impulses during the course of the operation; by gentle manipulation and sharp dissection; by the combination of all these methods the patient is protected from damage from every factor except those which exist in the diseased condition from which relief is sought (Fig. 33).

The *anociation*, however, does not end in the operating-room, nor with the return of the patient to his bed. Postoperative environmental conditions are no less essential than preoperative. To perform a shockless operation on a bad risk and then have the patient distressed and nagged by poor after-care is like putting tacks on a smooth pavement in the path of an automobile after driving it safely over rough roads. To achieve the shockless

operation the patient must be received and carried through a complete *anociation.* Not only the surgeon himself but also the resident staff, the anesthetists, the hospital officials, and the

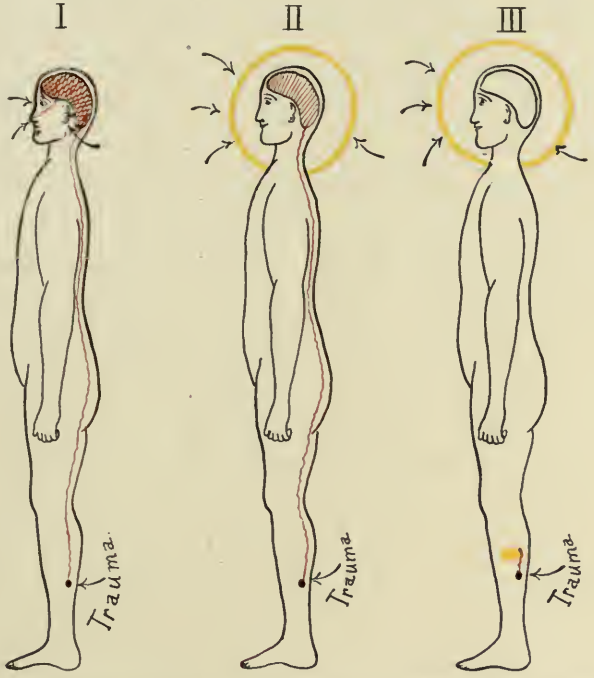


FIG. 33.—SCHEMATIC DRAWING ILLUSTRATING PROTECTIVE EFFECT OF ANOCIATION.

I, Conscious patient in whom auditory, visual, olfactory, and traumatic noci-impulses reach the brain. II, Patient under inhalation anesthesia in whom traumatic noci-impulses only reach the brain. III, Patient under complete *anociation;* auditory, visual, and olfactory impulses are excluded from the brain by the inhalation anesthesia; traumatic impulses from the seat of injury are blocked by novocain.

nurses must be specially trained; and, above all, it must be borne in mind that no detail is too petty for the attention of the surgeon himself.

GENERAL TECHNIC OF ANOCIATION

Morphin and Scopolamin.—To mitigate the preoperative anxiety and to facilitate the induction of anesthesia a solacing dose of morphin and scopolamin (usually morphin $\frac{1}{6}$ grain, scopolamin $\frac{1}{150}$ grain) is given an hour before the operation to all patients except the aged, the very young, and those whose feeble condition contraindicates the use of these narcotics. The use of morphin serves the double purpose of diminishing the preoperative psychic strain and of actually preventing, to some extent, the damaging of the organs of the kinetic system by the trauma of the operation.

That deep morphinization will almost completely prevent shock has been abundantly proved in both the laboratory and the clinic. A striking confirmation of this fact is found in the following case:

The patient was a woman forty-six years of age with obstruction of the bowels from a solid tumor which occupied the entire abdomen and caused distention greater even than pregnancy at term. This tumor had been explored six months previously by a skilful colleague who had wisely judged the case to be inoperable, the urgent condition of obstruction not being present at that time. When the patient came to us she was weak, emaciated, and was running a slight daily fever. Under *anociation* the abdomen was opened and a careful search was made for the obstruction.

The wide-spread adhesions and the actual inclusions of the viscera in the growth soon showed us that we could not relieve the obstruction without attempting the apparently impossible removal of the tumor. When this decision was reached the pulse had mounted to 142 and the respiration to 38.

The completion of the operation would mean the resection of the bladder and of part of the small intestine. Nerve blocking in these deep fused structures was impossible. Transfusion would be insufficient to relieve the situation. Death was certain if we

retreated and apparently equally certain if we proceeded. In no case could an added resource be more urgently needed.

It was at once decided to apply our laboratory findings regarding the protective effects of morphin. The operation was interrupted and morphin was given in $\frac{1}{4}$-grain doses at ten-minute intervals until the respiration had fallen from 32 to 12 per minute. We then resumed the tedious and difficult task of separating the huge, adherent, semimalignant tumor by means of sharp dissection. To accomplish this separation it was necessary to resect a portion of the small intestine, the entire fundus of the bladder, and several inches of the right ureter, the proximal end of which was implanted into the back by Bottomley's method. The tumor had been unable to gain a sufficient blood-supply through its original pedicle, and had, therefore, made many vascular connections with the neighboring organs, and consequently much blood was unavoidably lost during the operation. To counteract the resultant anemia a transfusion of blood from the patient's sister was given.

At the close of the operation and the transfusion the respiration ranged from 6 to 10 per minute and the pulse-rate was 134.

The patient was placed in bed in a modified Fowler position and sodium bicarbonate and glucose were given immediately by the drop method per rectum, while sufficient morphin was given in repeated doses during the first twenty-four hours to hold the respirations to 12 per minute. The patient made a splendid recovery from the operation.

The protective effect of morphin is remarkably exhibited in those cases of exophthalmic goiter in which some exceptional local condition causes a break in the complete *anociation* of the patient, as a consequence of which the pulse and respiration increase markedly during or after the operation. In these cases if morphin is given in repeated doses until the respiration and pulse are held

stationary or fall, the dangerous exhaustion of the patient will be avoided. *Provided always that the patient is not cyanosed,* morphin may be given at any time during or after the operation when it is seen that the patient's energy is being expended at too rapid a rate. It is best not to give morphin until the patient is out of the anesthesia.

Morphin is especially useful also in those cases of acute infection in which emergency operations must be performed. In such cases morphin affords a double protection—it protects the brain against the infection as well as against the operative trauma, the effects of which are increased, because during the activation of a toxin the brain thresholds are greatly lowered. Here also the morphin should not be given in one dose, but in repeated doses until the physiologic effect is produced. This point will be indicated by the reduction of the respiration to normal or less than normal.

In brief, by proper use, morphin, to a large extent, controls the metabolic processes. It should be added that it is not our intention to suggest an increase in the use of morphin in *average* cases, but to emphasize its usefulness when employed in physiologic dosage in certain *exceptional* cases.

Novocain.—Every division of a sensitive tissue, that is, of a tissue supplied with nociceptors, is preceded by the injection of novocain in 1 : 200 solution with adrenalin except in exophthalmic goiter cases. This is used routinely in all parts of the body, in all ages, in the debilitated and in the strong, in small and in extensive operations. Novocain is used in the smaller operations under all sorts of conditions not because there is any danger of shock, but because the incision through unanesthetized tissue may cause a change in the respiration and, in consequence, an uneven anesthesia; and second, because if novocain is used only occasionally the solution and the syringes will not always

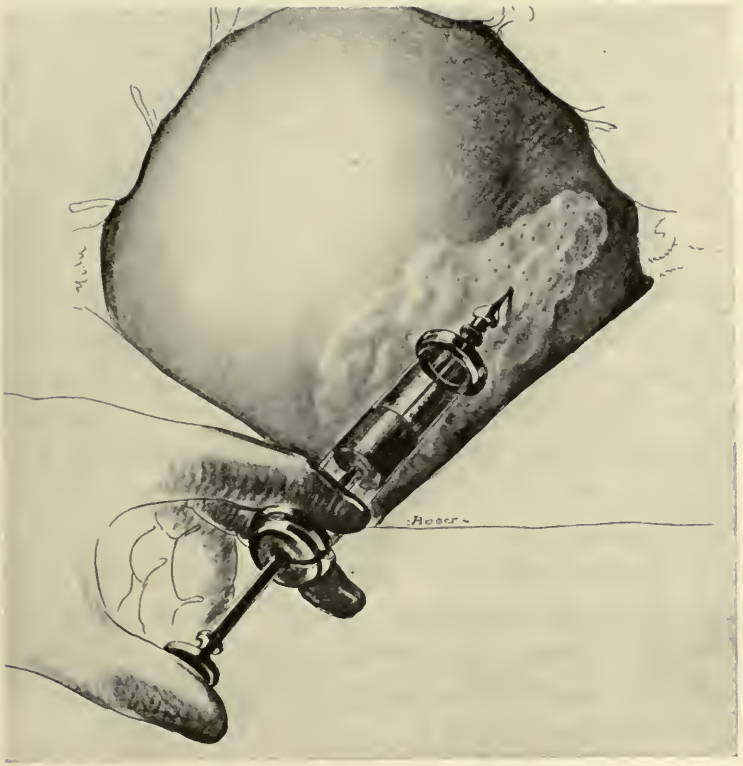


FIG. 34.—INFILTRATION OF NOVOCAIN BETWEEN SUPERFICIAL AND DEEP LAYERS OF SKIN. NOTE "PIG-SKIN" APPEARANCE.

be at hand. There are certain points of prime importance to be observed in the induction of local anesthesia: No nerve filament should be omitted; one might think of the local anesthetic as a stain and consider that only the stained parts are ready for the knife. The infiltrated parts should be subjected immediately to pressure, as firm pressure with the hand greatly increases the efficiency of the anesthetic and extends the localized area.

It is well to make the first infiltration between the superficial and deep layers of the skin in such a manner as to cause a pigskin appearance (Fig. 34). This is facilitated by putting the skin on tension and then, while making the injection, pushing the needle along *in* the skin parallel to the surface.

In many operations regional anesthesia is excellent—*i. e.*, in operations on the chest, in the abdomen, for hernia, for goiter, on the jaw, the blocking of the nerves supplying the operative field gives excellent results.

Experience in operating under local anesthesia alone is almost essential for learning how to use infiltration effectively in combination with general anesthesia, for the conscious patient promptly protests if the infiltration is incomplete. As a result of an abundant experience with conscious patients, the surgeon, even when operating on anesthetized patients, will automatically plan the operation and the handling of the tissues in the manner which would cause the least response were his patients conscious.

It is obvious that the anesthetic solution should be most carefully prepared and sterilized. In our clinic this is done as follows: Normal saline solution is prepared with distilled water and boiled for twenty minutes; to this a sufficient number of novocain crystals are added to make a 1 : 200 solution, which is then boiled for ten minutes each on two successive days; 15 mm. adrenalin to a small cup of the solution is added in all operations excepting for exophthalmic goiter.

When novocain is properly injected it anesthetizes the part immediately; the anesthesia lasts for approximately an hour; and it does not interfere with the healing of the wound. The efficiency of novocain is augmented by adrenalin.

Quinin and Urea Hydrochlorid.—On account of edema and perhaps some interference with wound healing the use of quinin and urea hydrochlorid is reserved for serious cases only. To minimize postoperative discomfort, especially in abdominal operations, quinin and urea hydrochlorid in $\frac{1}{6}$ to $\frac{1}{2}$ per cent. solution is injected *at a distance* from the wound. The effects of this local anesthetic last for several days, so that by its use the patient is protected from nocuous impulses from the operative field until the healing process has well begun. This local anesthetic can be safely used in all cases in which no infection is present, but is unsafe in the presence of infection because it to some extent diminishes the resistance of the tissues. Quinin and urea hydrochlorid usually causes some edema of the infiltrated part which may last for weeks, but which ultimately disappears. In our clinic the solution used is prepared by boiling distilled water for twenty minutes; then adding a sufficient number of sterile quinin and urea tablets to make a solution of the required strength, which in turn is boiled for ten minutes.

Moynihan has devised an excellent syringe with an obtuse-angled needle by means of which the quinin and urea hydrochlorid may be injected *at a distance* from the incision so that the entire operative field will be anesthetized for two days or more after the operation, while the wound itself is not exposed to the irritation of the quinin and urea (Fig. 35). In cases of advanced Graves' disease the infiltration of the field with quinin and urea hydrochlorid is markedly beneficial.

Gentle Manipulations: Sharp Dissection.—The phylogenetic facts upon which the *kinetic theory of shock* is founded indicate the

necessity for the use of the gentlest manipulations throughout the operation. In this respect the surgeon should at all times

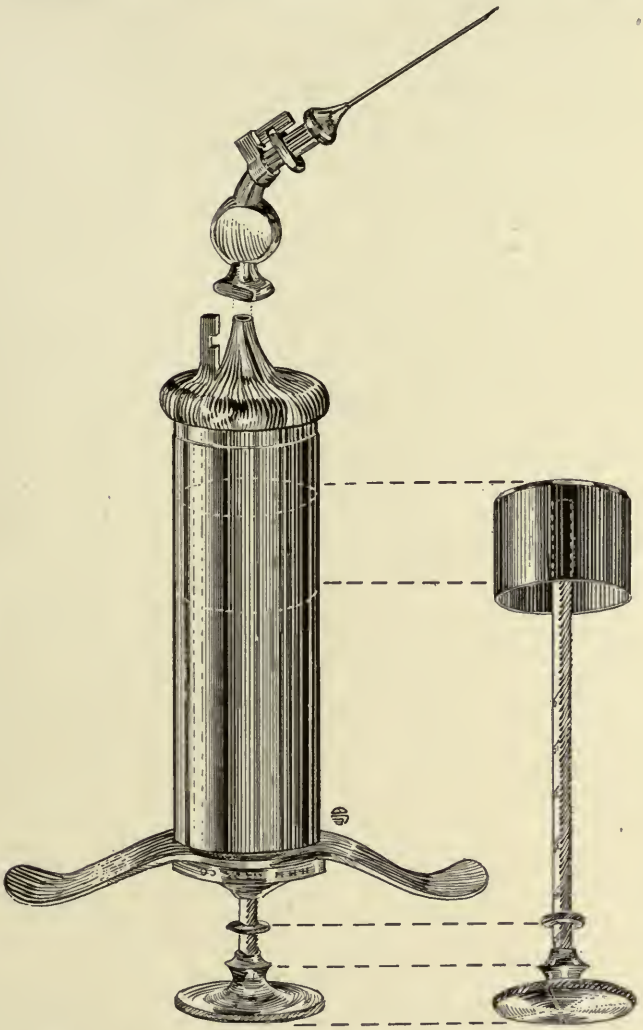


FIG. 35.—MOYNIHAN SYRINGE FOR THE INFILTRATION OF QUININ AND UREA HYDROCHLORID *at a Distance* FROM THE INCISION.

govern his movements as he would if the patient were to be conscious of each step in the operation. Pulling, tearing, and crushing

manipulations awaken phylogenetic noci-associations with consequent activation for defense, and exhaust the organs composing the kinetic system, especially the brain. In addition, actual coincident trauma is produced by traction on the tissues beyond the zone which is protected by the infiltration of the local anesthetic. On the other hand, the division of the tissues with a sharp scalpel is a form of injury which awakens less phylogenetic association and, in addition, produces the least amount of damage to the tissues. Gentle manipulation and sharp dissection produce the least amount of tissue injury, and therefore necessitate the minimum amount of healing. *Clean-cut wounds give the least postoperative discomfort.* It should be borne in mind also that trauma, by diminishing their vitality, predisposes the tissues to infection. For every reason, therefore, the tissue trauma should be as slight as possible.

CHAPTER VI

SHOCK AND EXHAUSTION, ANOCIATION, AND RESTORATION IN MILITARY SURGERY

Our researches on animals, which have extended through many years, have included experiments covering every cause of shock and exhaustion except those which were impracticable on account of their cruelty. This war, however, has provided ample human material to make good the deficiencies in laboratory researches caused by due consideration for the suffering of animals.

In our experiments we found that exhaustion (some forms of which we call shock) was caused by injury, fear, exertion, infection, worry, asphyxia, hemorrhage, loss of sleep, starvation.

In the war soldiers are being subjected to all these causes of exhaustion to a degree never produced in any laboratory. They are exposed to cold and wet and mud; to continuous worry and foreboding for long periods; to homesickness and depression; to the utmost hunger and thirst; to the annoyance of vermin; to nauseating odors; to general infection. They are subjected to the effects of high explosives; to every type of physical injury; to wound infection. They are buried alive.

Those exhausted soldiers whose good fortune it is to be taken promptly to the advanced hospital are relieved from physical pain and the stress of battle. Here they are warmed, are given hot drink, and are allowed to rest. In grave cases a transfusion of blood is given before a short deft opportune operation under nitrous oxid-oxygen.

But there are others who do not reach the advanced hospital promptly, in whom intracellular changes have been wrought by

the length and intensity of their exposure. These have a different appearance—present a different problem. The "shell-hole" man has a problem all his own.

The soldier marooned in a shell hole on No Man's Land may be as far from help as if he were across the sea. In such practical times good stretcher bearers are not exchanged for an incapacitated soldier. He has iron rations, but no water. He must drink the water from the shell hole. The sleep of exhaustion overtakes him. His wound swells during the night, becomes painful and infected; his food is gone; there is no more water and his fever is high. Now and again he may receive a new wound. The moments drag. He cannot die; he cannot live. Another night; another day; each growing worse and wearing him down—fever, pain, thirst, despair. After several days he sinks into a half-unconscious state of exhaustion.

He experiences no joy when he is dragged out of the shell hole by the stretcher bearers. The bone fragments grind—he is indifferent. He does not recognize the hot tea offered him at the advanced station. He is unconscious when he arrives at the advanced hospital. He is lethargic. His eyes are half-closed. He is cold, pulseless, wet, clammy, yellow tinted, shrunken faced. The wound contains mud and clothing and is infected. This is not an exceptional, not an unusual case, but common after a great battle. The condition varies with the character of the wound, the kind of weather, the nature of the place which has offered concealment, the possibility of obtaining food, the type of infection—pyogenic, gas gangrene, tetanus. The onset of tetanic convulsions may occur in a dark night when the exhausted soldier is half-submerged in bottomless mud (Flanders Fields), the vigorous convulsive movements deepening his position until the advent of the last beneficent convulsion which completes the welcome closure of the soft mud over him, ending his

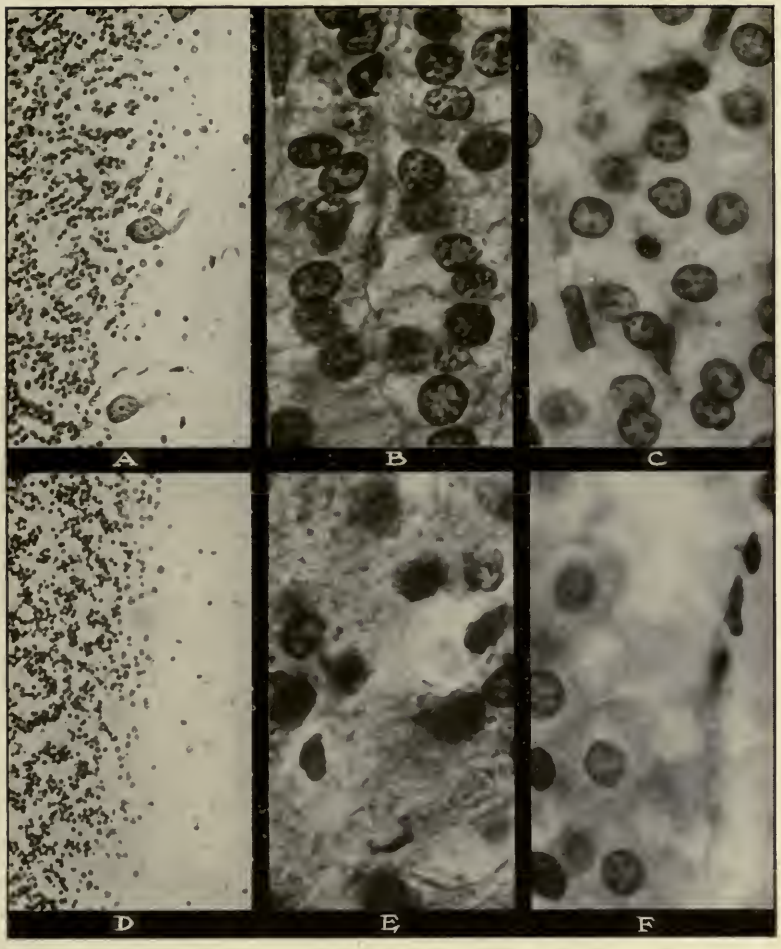


FIG. 36.—EFFECT OF COMBINED STIMULI, CHIEF AMONG WHICH WERE INSOMNIA, EXERTION, AND EMOTION, ON THE BRAIN, ADRENALS, AND LIVER OF A SOLDIER WHO DIED FROM EXHAUSTION. Case I (A and D from photomicrographs × 310; B, C, E, and F from photomicrographs × 1640.)

A, Section of normal cerebellum. B, Section of normal adrenal. C, Section of normal liver. D, Section of cerebellum of exhausted soldier. E, Section of adrenal of exausted soldier. F, Section of liver of exhausted soldier.

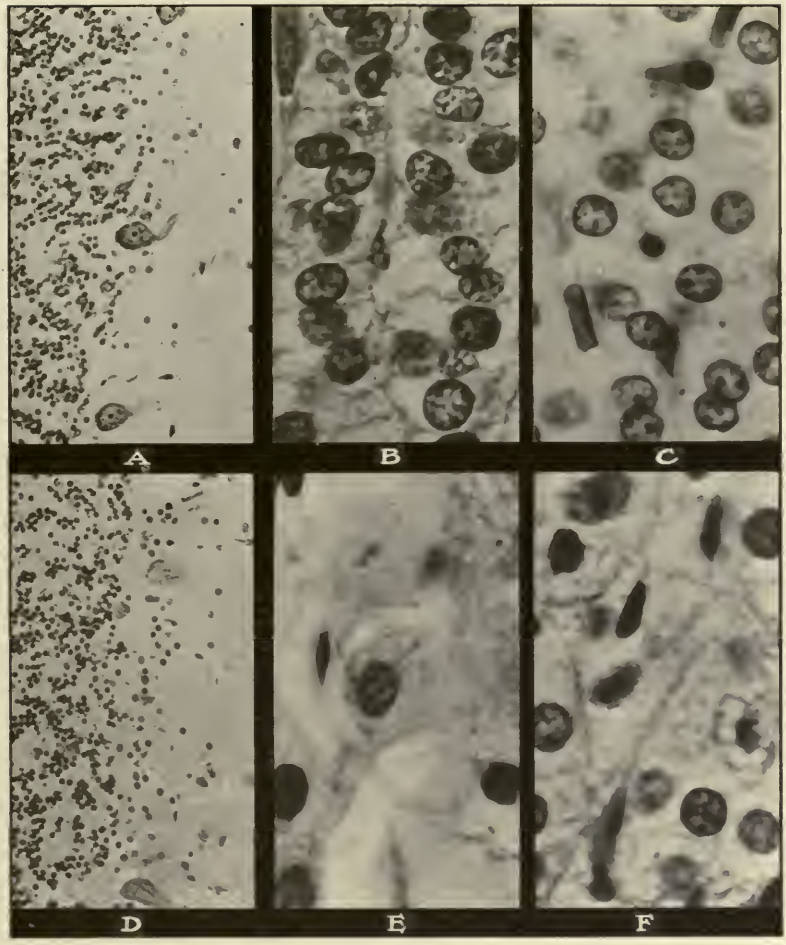


FIG. 37.—EFFECT OF COMBINED STIMULI, CHIEF AMONG WHICH WERE INSOMNIA, EXERTION, AND EMOTION, ON THE BRAIN, ADRENALS, AND LIVER OF A SOLDIER WHO DIED FROM EXHAUSTION. Case II (A and D from photomicrographs × 310; B, C, E, and F from photomicrographs × 1640.)

A, Section of normal cerebellum. B, Section of normal adrenal. C, Section of normal liver. D, Section of cerebellum of exhausted soldier. E, Section of adrenal of exhausted soldier. F, Section of liver of exhausted soldier.

pathologic strivings. Even the slightly wounded may be drowned in mud. Sometimes they are rescued, sometimes they gravitate and join the throng underneath; for many hundreds, perhaps thousands, of wounded soldiers have been swallowed by the morass.

Exhaustion in every form is seen in the wake of battle. The surgeon sees only the more fortunate cases. The untold stories need not concern us; the every-day facts are sufficient (Figs. 36, 37).

From their personal experience in the observation, examination, and treatment of these cases the authors have drawn the following conclusions:

Anociation has proved to be of the utmost value. These patients require *an intracellular resuscitation*. The intracellular mechanism is far less impaired in acute shock of short duration. The treatment that succeeds well in the acute case may not succeed in the case of the shell-hole man. We are convinced, therefore, that in addition to the treatment outlined for the case of shock in the civil hospital, additional measures must be employed. The specific is not yet at hand, but opportune treatment carefully planned to meet this or that indication will save many. In these cases nitrous oxid-oxygen is a remarkable means of *anociation*, but while nitrous oxid-oxygen alone does well, the addition of regional or sacral anesthesia provides still another factor of protection.

CHAPTER VII

ANOCIATION IN ABDOMINAL OPERATIONS

General Technic.—Our associates, Drs. F. E. Bunts, H. G. Sloan, and the members of the Resident Staff of Lakeside Hospital, have performed 12,382 abdominal operations, 9424 before the use of anociation was inaugurated and 2958 under anociation. The striking improvement in our results since the adoption of these methods furnishes us with the incentive to try to achieve a technic which will assure an even more complete anociation.

Technic.—Except to the very young, the aged, and patients with depressed vitality, morphin ($\frac{1}{6}$ grain) and scopolamin ($\frac{1}{150}$ grain) are administered one hour before the operation. The young, the old, and certain handicapped patients are not given this preoperative sedative dose. In nitrous oxid-oxygen we have an efficient preventive of shock; but in abdominal operations the anesthesia is so light that muscular rigidity is produced unless local anesthesia is used and most gentle manipulations are employed. The rigid abdomen under nitrous oxid-oxygen is more the problem of the surgeon than of the anesthetist.

The skin is infiltrated with novocain in 1 : 400 solution in such a manner as to produce a broad, white elevated strip of skin within which—*strictly within which*—the incision is made (Fig. 38). The razor-edged knife divides the skin and underlying fat. As fat is but sparsely supplied with nerves, this tissue may be divided down to the external fascia without novocain infiltration.

The external fascia is next infiltrated and is divided by the controlled passage—*not sweep*—of a sharp scalpel, and then, in succession, the muscles, the posterior sheath, and the peritoneum are anesthetized and divided (Figs. 39, 40).

FIG. 38.—ABDOMINAL OPERATIONS: INFILTRATION OF SKIN AND SUBCUTANEOUS TISSUES WITH NOVOCAIN.

If the patient is a grave risk, and if there is no infection, then, as soon as the abdomen is opened, quinin and urea hydrochlorid in $\frac{1}{6}$ to $\frac{1}{2}$ per cent. solution is used in a massive infiltration of the abdominal wall *at a distance from the incision,* the infiltration being so complete that the entire operative field is physiologically severed from the brain (Fig. 41). The effect of the quinin and urea hydro-

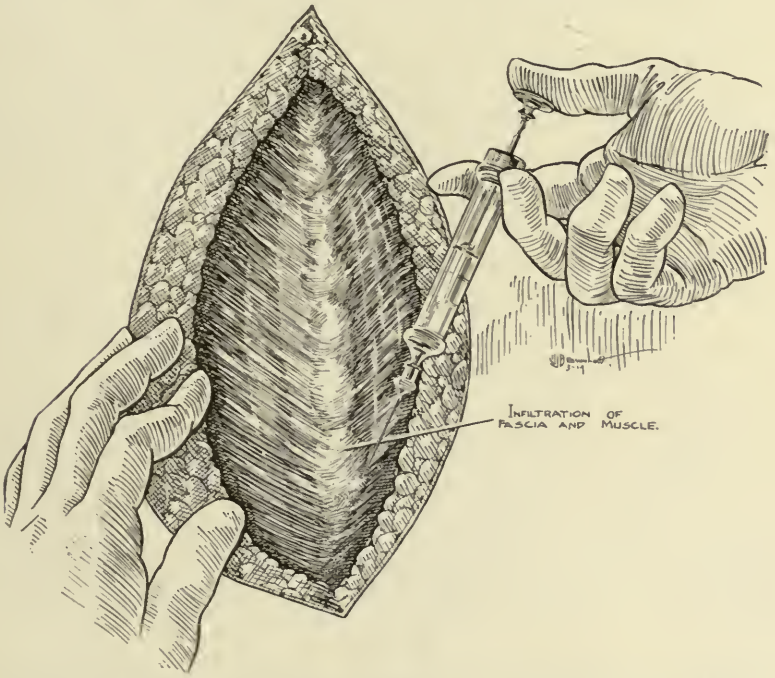


Fig. 39.—Abdominal Operations: Infiltration of Fascia and Muscle with Novocain.

chlorid lasts for two days or more and minimizes the postoperative shock and gas-pain. It must be repeated that quinin and urea hydrochlorid are used *in only the grave risks.*

If the principle of anociation be carried out in every detail, then, no matter what may be the location or the length of the abdominal incision, the intestines will remain within the abdominal

cavity and the abdominal muscles will be completely relaxed (Fig. 42). Under these conditions the entire abdomen may be explored without causing any contraction of the abdominal muscles. If the incision be long, the entire wall may be elevated with the warm, moistened, gloved hand, and most of the viscera

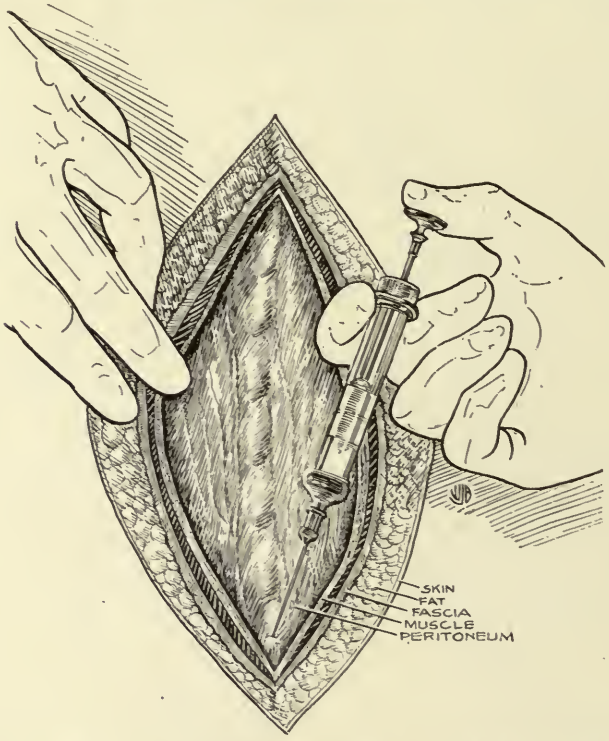


FIG. 40.—ABDOMINAL OPERATIONS: INFILTRATION OF POSTERIOR SHEATH AND PERITONEUM WITH NOVOCAIN.

inspected. The hand may then go gently but completely over every viscus, and explore every nook and corner of the abdomen without disturbing the original complete muscular relaxation.

It may happen, however, in spite of biologic strategy that the existing condition may make it impossible to avoid the stimulation of noci-ceptors, so that muscular contractions may be excited.

In such a case the nitrous oxid-oxygen should *not be pushed an atom beyond the pink stage,* but ether should be added until the needed relaxation is reached; a few minutes and but little ether are usually sufficient to attain this end. The nitrous oxid-oxygen apparatus should have an ether attachment, to be used to *supplement* nitrous oxid, not to displace it.

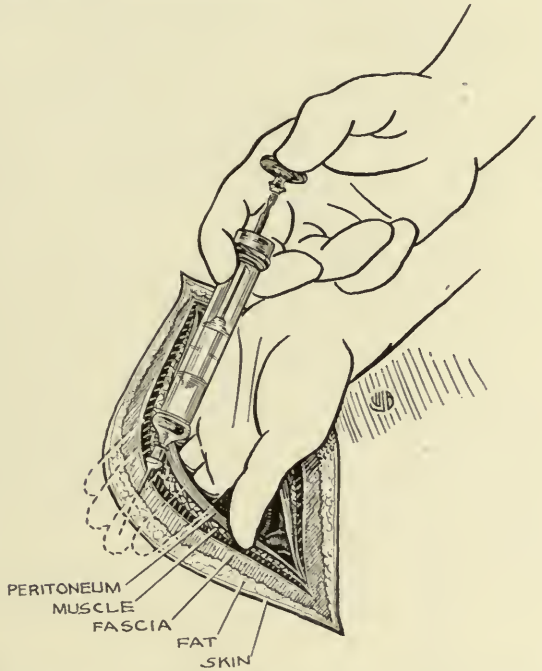


FIG. 41.—ABDOMINAL OPERATIONS: INFILTRATION WITH QUININ AND UREA HYDROCHLORID *at a Distance* FROM THE INCISION.

Owing to the entire relaxation of complete anociation but few, if any, intra-abdominal pads are required. Nowhere is the law of consequences more truly exemplified than in abdominal operations. In no instance does the punishment more truly fit the crime. Sow roughness and reap a harvest of postoperative distress.

In the following chapters we shall deal with the practical

application of the principle of anociation in various types of abdominal operations. The most difficult and critical abdominal operations, which carry the highest mortality, are those for the repair of the perforating gunshot wounds received in war. We therefore include the following note made by one of the most experienced and careful British surgeons. The operations which he reports were all performed at the same casualty clearing station, the patients were similar in type, the distance from the place in the fighting line where each was wounded was approximately the same, the anesthetic in each case was administered by the same anesthetist. These conditions afforded an unusual opportunity to compare the results secured with and without anociation.

NOTE ON GAS OXYGEN AND LOCAL ANESTHESIA IN OPERATIONS FOR GUNSHOT WOUNDS OF THE ABDOMEN

By Captain Douglas C. Taylor, R. A. M. C.

Until the summer of 1917 my colleague, Captain G. Marshall, invariably gave ether for my laparotomies for gunshot wounds of the abdomen. No series of 100 consecutive cases showed a recovery rate of much over 50 per cent.

During the summer and autumn of 1917 I did 101 laparotomies for abdominal wounds, and nearly half of them were given nitrous oxid and oxygen, combined with infiltration of the abdominal wall with eucain or novocain. The more serious cases—*i. e.*, those with rapid pulse and low pressure—were nearly all done by this method.

Of this series, 27 died at the casualty clearing station, and 74 were evacuated to the Base; of the latter, there have been only two deaths, both from secondary hemorrhage—one from the kidney and the other from the rectum and buttock.

Various incisions were used, *i. e.*, median, paramedian and transverse or oblique, subcostal in both upper and lower abdomen. Relaxation was invariably good, provided the deeper layers of the abdominal wall had been carefully infiltrated. Very occasionally a little ether was given to facilitate closure of the abdomen,

FIG. 42.—COMPLETELY RELAXED ABDOMINAL WALL AND INTESTINES, THE RESULT OF *Anociation*.

always done by suturing in layers. We found this type of anesthesia well tolerated in combined chest and abdominal wounds, also in patients who were suffering from poison gas. Both types give a very high mortality with ether anesthesia.

These much improved results must also be attributed in part to transfusion of whole blood, which was practised after the operation in the more exsanguinated patients.

The following notes of a case will demonstrate the value of the combined method:

1830—Pvt. C., aged thirty-four, admitted 8/10/'17. Wounded six hours previously by high explosive shell. Very pale and restless, extremities cold, no palpable pulse at wrist. Had vomited coming down. Single entry wound left buttock, no exit wound. Abdomen rigid and tender.

Patient put in hot-air chamber. Two hours later patient was warm, but still no pulse palpable at wrist. Blood-pressure 68.

Operation.—Gas and oxygen and local infiltration of abdominal wall with 1 per cent. novocain solution. Median laparotomy below umbilicus. Abdomen full of blood. Three large rents found in a loop of the jejunum, also three holes in its mesentery. Eight inches of the bowel resected, end-to-end anastomosis. Abdomen mopped dry and closed without drainage. Blood-pressure would not register at end of operation.

The patient was immediately transfused with 1200 c.c. of whole blood by Captain Rogers of No. 9 General Hospital. After transfusion pulse at wrist 120, and blood-pressure 100.

Patient had hiccup lasting for a week, which required morphin (grain $\frac{1}{2}$) daily to keep it controlled. He gradually picked up strength and was moved to the Base thirteen days after operation. He has since been reported as doing well in England.

Note.—The last Inter-allied Conference adopted the method described above as the method of choice in abdominal operations.

CHAPTER VIII

ANOCIATION AND PERITONITIS

What is peritonitis? If peritonitis is the adaptive protective response of the organism to infective invasion of the peritoneal cavity, then it would appear that peritonitis is no less an evolved adaptive phenomenon than is running away from danger or withdrawing the hand from injury. This protective response of the organism against peritoneal invasion may be so intense as in itself to cause death. That such a death is analogous to death from traumatic shock is proved by the fact that as death from trauma cannot occur when the protective response to trauma is prevented by local or regional anesthesia, and as the response to trauma is minimized by heavy morphinization, to the same extent and for the same reason heavy morphinization protects the organism against the effect of infection.

What evidence is there that peritonitis is an adaptive and protective response against infection? First, although the main, if not the only, defense against the bacteria that cause infection is phagocytosis, the phagocytes are not at all times present in the tissues in sufficient numbers to guard against infection, but must be brought to the point of attack by the blood-stream. It takes hours, even a day or more, to mobilize an effective army of phagocytes; therefore it is vitally important that the point of infection be localized. It is known that the peritoneum is capable of overcoming almost any infection if the infection can be localized; but how can an infection be localized in the midst of many feet of slippery, ceaselessly moving intestines? If digestion and absorption are to go on, the intestinal peristalsis must be continuous. To meet the requirements of localization, therefore, one would

suppose that there must have been evolved an adaptation to arrest the intestinal peristalsis. One of the first responses to peritoneal infection is paralysis of the intestine, but even with the quiet of intestinal paralysis, how can a point of infection be held localized in the presence of the smooth, slippery peritoneal lining of the entire abdominal cavity which is swung back and forth with each respiratory movement, with each change of posture of the body? To prevent movement of any and all kinds the beneficent protection of pain was evolved. In the presence of peritoneal infection movement of every kind causes acute pain; and pain prevents body movements. But when the body and respiration have become quieted by pain the paralyzed viscera would still slide about and spread bacteria among the neighboring coils; to meet this requirement we may suppose the sticky exudate was evolved to glue together and seal in the area of infection. Thus the abdominal muscles are stilled, the diaphragm limited in motion, the whole man is quiet, his intestines are paralyzed, and the infected coils are stuck together.

The urgent need of the mobilization of a vast army of phagocytes we may suppose led to the evolution of the adaptive response which provides a vast blood-supply to the infected area. If complete paralysis exists, then digestion and absorption cannot proceed, and the food in the stomach and the intestine would decompose into toxic elements. To meet this danger a beneficent anorexia and vomiting were evolved. But the contents of the alimentary canal, already past recall by vomiting, may cause trouble, and the gastric juice and bile and pancreatic juice may accumulate. The intestinal tube could easily empty itself by acute diarrhea, but the acute peristalsis would spread the infection; hence, we may suppose the more disagreeable and less efficient reverse peristalsis and vomiting were evolved as providing greater net profit.

If it is highly important that the infection should not be spread, that the soft plastic fixation should not be broken up, then general bodily mobility must be arrested, and a mechanism which wholly prevents pressure upon the abdomen evolved. For this purpose the extremely efficient and beneficent exquisite tenderness was evolved.

The body must always maintain a standard of chemical purity, and if foreign proteins are introduced, these must be destroyed. For this purpose we presume still another mechanism was evolved —chemical receptors—the adequate stimuli of which are *foreign proteins, bacterial toxins,* etc. As a result of adequate stimulation by bacterial toxins the brain is activated. As a result of the activity of the brain, increased metabolism and increased heat are produced. With each degree Centigrade of elevation of temperature the total chemical activity is increased 10 per cent. It is believed that foreign proteins from bacteria are split up more readily than are the living protein molecules of the individual; for this reason there was evolved this remarkable chemical protection against the foreign proteins of infection, in reality a purification by forced oxidation—purification by biologic fire.

With the increased metabolism the acid by-products are correspondingly increased, and death would occur but for the fact that carbon dioxid causes increased respiratory activity, which leads to its rapid elimination and thus prevents acidosis. This explains in part the increased respiratory rate in peritonitis; the other cause being the fact that the abdominal rigidity prevents the full use of the lower lobes of the lung. The increased demand for lung ventilation, together with the diminished functional capacity, is met by a greatly increased respiratory rate.

Whenever the organism is deluged with waste products, as in peritonitis, the circulation is speeded up to facilitate elimination, hence the quickened pulse; but vast quantities of blood have been

beneficently diverted from the main circulation to the abdominal circulation, hence the small pulse. The intake of fluid is diminished, and the increased loss of fluid by the beneficent act of votmiing, combined with the diversion of blood causes the shrunken facies. Because of the diminished blood—diminished fluid—the face may finally become cold. The vast amount of waste products demands the greatest activity of the mechanism of elimination, hence the perspiration. How beneficent are some of the intensely disagreeable means which nature had to employ to make wilful, careless, unintelligent man save himself!

What examples of adaptation are the phenomena which constitute peritonitis! And if we view these phenomena as adaptations, we shall *be more likely to play into the hand of nature—and not against her!*

All this complicated mechanism is operated through association, just as the response to trauma and to an emotion are operated through association. But the surgeon, by excision of the focus of infection, by repair of perforations or rents in the intestinal walls, by establishment of adequate drainage, by Fowler's position and assurance of physical rest has in part fulfilled the purposes of the adaptive mechanism. Therefore, if the further drain upon the organism of activity of the whole mechanism of defense can be obviated by abolishing the stimuli which call it into action, by so much will the vitality of the patient be conserved.

The activity of this protective mechanism is evoked by the bacterial toxins which as adequate stimuli activate associative memory. Associative memory is diminished or abolished by morphin. Emotion is abolished by morphin as are also pain and muscular action, and in like manner and to the same degree the associative memory evoked by an abdominal infection is abolished by sufficient morphin. Just as a preliminary dose of morphin is used as an essential step in the anociated operation, so will it

serve to accomplish the "peritonitis-less" abdominal infection. The value of morphin in large doses was recognized by Alonzo Clark, whose method is certainly the most effective non-surgical treatment of peritonitis. When by its use anociation of the infection is added to anociation of the operation the most efficient surgical treatment is achieved. In the wounded soldier in particular, in whom associative memory of cold and wet and mud, of continuous worry and foreboding, of homesickness and depression, of hunger and thirst, of vermin, of noisome sights and sounds and odors, add to the menace of his abdominal infection, deep morphinization is of paramount value.

The essential points in the anociated treatment of abdominal infection are the following:

1. Nitrous oxid-oxygen.
2. Anesthetized incision.
3. Accurate clean-cut operation, awakening the least possible associative memories of either infection or trauma.
4. Adequate drainage.
5. Fowler's posture.
6. Vast hot packs over entire abdomen spreading down over the sides.
7. Five per cent. sodium bicarbonate, with 5 per cent. glucose by rectal tap, continued as long as it is tolerated.
8. Primary lavage of stomach, repeated only if indicated (it will rarely be indicated if *anociation* is complete).
9. From 2000 to 3000 c.c. of normal saline subcutaneously every twenty-four hours until the period of danger is past.
10. Morphin hypodermically until the respiratory rate is reduced to from 10 to 14 per minute; hold to this rate until danger is past.

DON'T!

Don't make multiple abdominal incisions.

Don't provoke even the least needless disturbance of the protective mechanism against peritonitis.

Don't break up protective adhesions beyond the slightest extent absolutely required.

Don't try to move the bowels in the acute stage. The bowels know when it is safe to move, especially with a continuous Murphy drip. Use enemata, not cathartics, at the proper time.

Don't hesitate to give enough morphin—the more serious the case, the more morphin will be required.

Don't fail to note the hope expressed by the *pulse* of the morphinized patient as contrasted with the dry tongue and shrunken face and half-closed eyes, which are morphin phenomena, not peritonitis phenomena.

Don't think of the morphin habit; it cannot occur in such usage.

Don't continue morphin beyond the critical period—usually past in from one to four days.

CHAPTER IX

ANOCIATION IN ACUTE AND CHRONIC APPENDICITIS

In our series of 6495 cases of appendicitis we have encountered many strange circumstances. Perhaps no surgical disease has such a repertoire of vagaries. We have found an acute appendix in a hernia; attached to the gall-bladder; in the left pelvis; in the left iliac fossa; with the tip near the spleen; attached to the stomach. We have mistaken appendicitis for cholecystitis, for duodenal or gastric ulcer, for stone in the ureter, for stone in the kidney, for salpingitis, for diverticulitis. Chronic appendicitis has led to the suspicion of cancer; has been confused with neurasthenia and intestinal auto-intoxication.

The vagaries of abscesses of the appendix are no less marked. We have seen them retroperitoneal, in the left pelvis, opposite the kidney, in the subgastric area, in the left iliac fossa, in the splenic area. We have seen these abscesses point into the various parts of the intestine, into the bladder, into the ureter. We have seen the tip of the appendix left in the bladder, having been carried in with the penetrating abscess and kept behind by the urethra. We have seen an abscess of the appendix point into the hip-joint and burrow down into the popliteal space. We have seen a slight local lesion with fatal bacteriemia. We have seen an abscess burrow up and penetrate the diaphragm, the pleural cavity, and the lung, whence it was coughed up and the patient cured.

If we wished to make a complete discussion of appendicitis it would be necessary to throw out a wide net to embrace its versatile manifestations. In this connection, however, we wish to consider especially only the every-day acute form, and shall discuss the average rather than the exceptional case.

First of all, we realize that the results secured by surgeons everywhere have improved, but our own results have been so completely changed by a certain grouping of methods that we shall make the factors, to meet which these methods were planned, the special subject of our discussion. The cause of death from appendicitis is infection—local, general, pylephlebitis, or bacteriemia. Whatever may have been accomplished in the treatment of other forms of infection, there has been found no successful method of attack against bacteriemia *once it has become established.* Bacteriemia and pylephlebitis are quite *preventable,* however. Since we have adopted and followed fully the plan outlined above we have performed 409 operations for acute appendicitis between deaths. This series is believed to be large enough to cover chance results.

The adopted plan of treatment includes:

(*a*) Elimination of the damage of the inhalation anesthetic and elimination of the effect of surgical trauma.

(*b*) Special precautions against the occurrence of secondary abscesses.

(*c*) Prevention of pylephlebitis and bacteriemia.

(*d*) The anociated treatment of peritonitis as outlined in the preceding chapter.

The *anesthetic* is always nitrous oxid-oxygen—never even short ether, never supplemental ether. It is best also to use a local anesthetic in the abdominal wall.

Pylephlebitis.—This serious complication has been well mastered by a simple, but fundamental change in treatment, viz., all surgical measures are withheld, and the patient is put under the dietetic and hygienic treatment for tuberculosis, so perfectly worked out by the internists. The patient is kept on a porch of the hospital as far as practicable, night and day, and nourishment is forced. Under this treatment there will rarely be a death. The time required for convalescence is about twelve weeks.

Bacteriemia.—As we have said, the only method of dealing with bacteriemia is to prevent it by prompt early operation, by breaking up adhesions after vascularization.

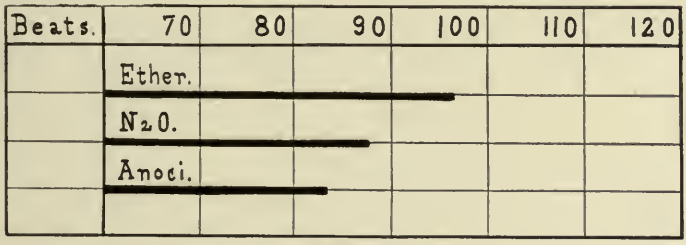
In acute appendicitis we direct that the patient be propped up in bed, in the ambulance, in transit to the operating-room, on the operating-table, *en route* from the operating-table to his bed, in bed until the danger of spreading infection is past. *The patient sits up throughout the progress of the disease.*

In these acute cases the incision is always over the center of the most tender area, always intermuscular. The peritoneal cavity is approached with the utmost care. If the abscess is localized, the operation is ended when the abscess is opened and gently explored. If the pus is free, then, regardless of the position of the appendix, the cigarette drain is carried down to *the left side* of the pelvis; the drain is carried along the bottom of the right pelvis, continues along the parietal peritoneum, and comes out at the lower end of the McBurney incision. This leads the pus from the left as well as from the right pelvis up to the opening. The Fowler position drains all free pus down into the pelvis, the cigarette drain directs the pus out of the pelvis, out of the abdomen, hence there are no residual abscesses in this territory. If the abscess is in the right loin, drain directly; this drain is not disturbed until the entire abdomen has settled down. The acutely inflamed appendix is picked up with the utmost gentleness, tied off near the cecum, and excised—no invagination—nothing more. The cecum is left unmoved; it is not placed anywhere; it is allowed to stay where it is or to go its own way.

If there is a walled-off abscess, then the abscess is cautiously opened at its center, wherever that center is—McBurney, left, median, hypochondriac, umbilical—the abscess is opened in the center of the mass, the center of the rigid area and of the tender area. The appendix is tied and cut off wherever it is found. The cecum is not looked for—is not moved.

The common cause of secondary abscesses, pylephlebitis, and bacteriemia is the opening up of absorption areas by the operation. The more careful we are, therefore, the more completely we respect nature's defense, the fewer will be these complications.

We have found that in the great majority of cases of acute appendicitis the appendix is removable. Otherwise after the patient has recovered and the wound is healed—and such wounds soon heal because they have no complications—the appendix may be removed by a clean intermuscular incision. The second operation is not indicated if necrosed portions of the appendix come away in the abscess.



The Pulse.

Each heavy line represents the average 5 P. M. pulse-rate of 10 patients during the first four days after operation.

FIG. 43.—COMPARATIVE CLINICAL RESULTS OF CONSECUTIVE APPENDECTOMIES PERFORMED UNDER ETHER ANESTHESIA, UNDER NITROUS OXID-OXYGEN ALONE, AND UNDER COMPLETE ANOCIATION.

The value of *anociation* in the acute abdominal infections is most strikingly illustrated by a comparison of the pulse-rate during and after operations in cases of acute appendicitis.

A study of 45 consecutive *ether cases* before the adoption of anociation showed an average *increase* of 8.4 beats in the pulse-rate in the first twenty-four hours after operation, and an average *increase of 15.4 beats* during operation; while the 45 consecutive *anociated* cases studied showed a *fall of 2.26 beats* in the first twenty-four hours after operation, and a *fall of 1.22 beats* during operation (Fig. 43).

CHAPTER X

ANOCIATION IN OPERATIONS ON THE STOMACH

THE study of the 600 operations for lesions of the stomach in our combined records show that two prime factors determine the result of gastric operations:

1. The state of partial starvation.

2. The degree of debility produced by the toxins of cancer and by hemorrhage.

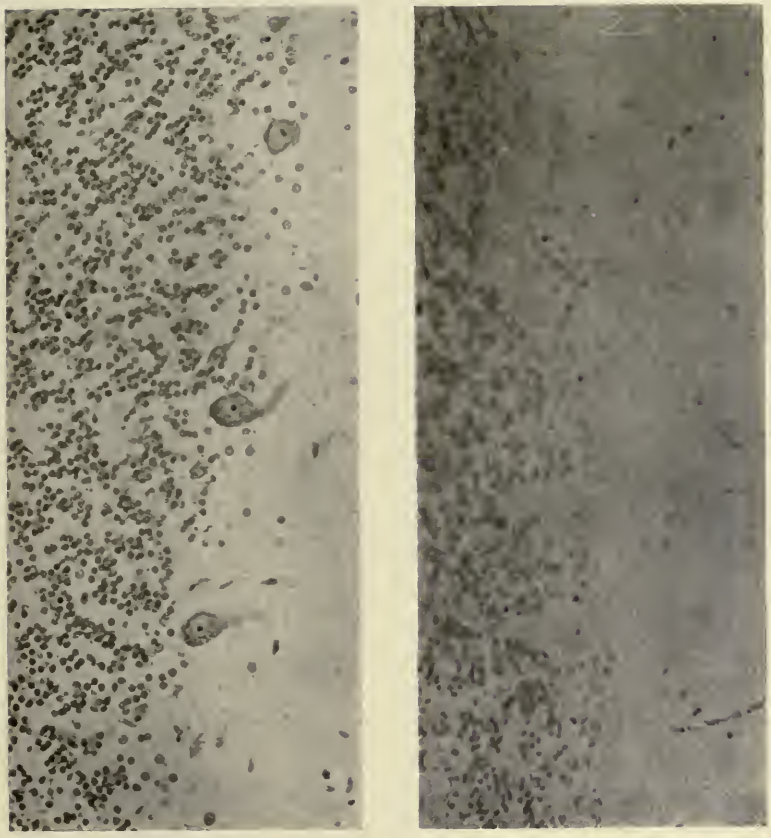
Our researches have shown that starvation and advanced cancer produce marked intracellular changes in the brain (Fig. 44), and it is a common experience that these two conditions are extremely unfavorable for surgical operations. Yet even in these states splendid results are secured by a strict adherence to the principles of anociation.

The following are the cardinal points to be observed in the anociated gastric operation:

1. The general condition of the patient is improved prior to operation by the administration of large quantities of sodium bicarbonate and glucose (5 per cent. of each) by rectum; and if pyloric obstruction is marked, by the subcutaneous injection of much water.

2. If there is marked anemia, give an adequate transfusion of blood.

3. If the risk is extremely grave, use nitrous oxid-oxygen only to the extent of analgesia, and depend mainly on local anesthesia. If the risk is fair, proceed as usual for abdominal operations.



A B

FIG. 44.—EFFECT OF CARCINOMA ON BRAIN CELLS. (From photomicrographs × 310.)

A, Section from normal human cerebellum. B, Section from cerebellum of patient who died of carcinoma.

4. Make an ample incision so that the operation may be taken to the stomach; do not take the stomach out unless it will come out easily without being pulled.

5. If there is a cancer-like mass, and the hazard is great, then at the first operation make only a gastro-enterostomy; otherwise, complete the operation in one séance.

6. In case of a two-stage operation, the resection may be made after the nutritional balance is well established, usually in about a week.

7. In the second operation not only will the resection be made with little disturbance, but as a result of the preliminary gastro-enterostomy there will be a strong mobilization of immune forces against infection in the operative field.

8. In certain cases it is impossible to differentiate cancer from ulcer by the symptoms and history, by *x*-ray examination, by palpation, even microscopically. Thus in 4 of our cases the entire mass that at the time of the first operation appeared to be cancer disappeared before the second operation, so that the resection was not required. Had the entire operation been performed at the first stage not only would the hazard have been great, but a needless operation would have been performed.

9. In cases of cancer we have found in the second stage of the operation that the rest provided by the preliminary gastro-enterostomy has reduced the size of the growth by diminishing the inflammatory tissue.

10. In the resection, if adhesions are found, *divide them with a sharp knife.* Make all dissections with *a sharp knife.*

11. Make a wide excision of the tumor.

12. Use round needles for suturing the stomach.

13. Avoid postoperative hemorrhage by using the cobbler stitch (Fig. 45).

14. Tie the interrupted sutures lightly.

15. Should there be postoperative vomiting, use the stomach-tube promptly.

16. Usually less postoperative disturbance is caused by the second and larger operation than by the first.

17. After the resection take especial precautions to keep the patient warm, and to keep up a good nutritional and water balance. The two-stage operation gives splendid opportunity for this

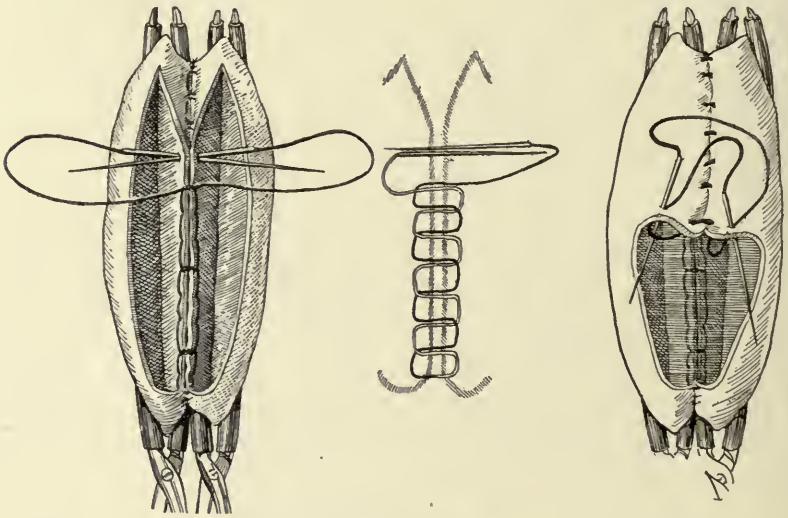


FIG. 45.—THE COBBLER STITCH.

because the physiologic adjustment resulting from the gastro-enterostomy occurs before the resection is made.

18. Convalescence is usually uneventful.

DON'T!

Don't give an acidosis-producing anesthetic to a patient on the verge of acidosis.

Don't drag heavily on the stomach.

Don't explore the abdomen after completing a gastrectomy.

Don't perform multiple operations in addition to the operation on the stomach.

Don't hesitate to make wide transverse incisions if the field of operation is not clear and convenient.

Don't use silk in a gastro-enterostomy excepting for light interrupted sutures.

Don't use cutting needles.

Don't fail to make the anastomosis at the point where the anastomosed viscera will lie in comfortable approximation.

Don't make a long intestinal loop.

Don't put a drain in contact with the line of sutures.

CHAPTER XI

ANOCIATION IN OPERATIONS ON THE GALL-BLADDER AND DUCTS

The value of anociation in gall-bladder operations is demonstrated by the reduction in the mortality and postoperative morbidity shown by a study of the 1213 operations on the gall-bladder and ducts which appear in our tables, 833 before and 380 since the adoption of anociation.

Cholecystectomy, Cholecystotomy.—If the general condition of the patient does not contraindicate, cholecystectomy should be performed. If there is stricture of the cystic duct; if decubitus in the cystic duct or an ulcer has resulted from impacted stones; if the wall of the duct is inflamed; if the wall of the gall-bladder is thickened or infected; even if the gall-bladder appears normal but there has been a severe infection; if there is much gritty débris in the gall-bladder; in short, if any local condition exists which predisposes to gall-stones or infection, then cholecystectomy should be performed.

The following precautions, in addition to anociation, ensure a shockless operation:

(*a*) Provide an absolutely free exposure of the operative field (1) by making the incision long enough, (2) by augmenting the primary incision when necessary by a right or left transverse incision.

(*b*) If nitrous oxid-oxygen and local anesthesia alone do not give sufficient relaxation for the development of the field, then supplement with sufficient ether, but only during the necessary period.

(*c*) Through *finesse* carry the dissection down to the gall-bladder, so that good technical opportunity will be afforded without the necessity for much damaging dragging and pulling and manipulation.

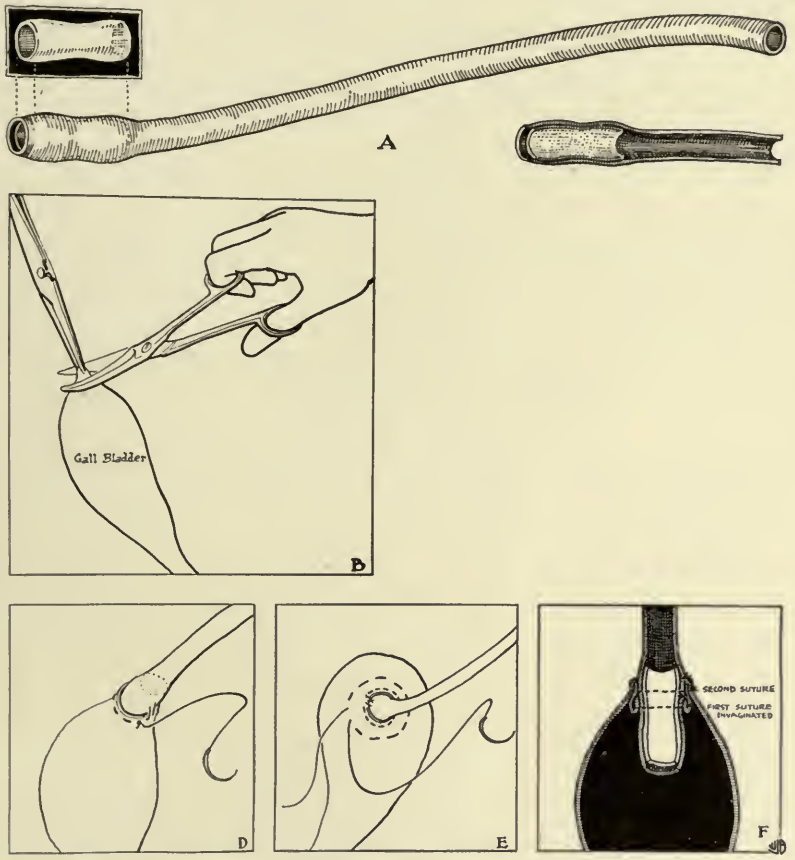


FIG. 46.—A DEVICE FOR FACILITATING DRAINAGE OF THE GALL-BLADDER

(*d*) As a rule begin at the fundus and make a sharp-knife dissection of the gall-bladder from the liver all the way down to the cystic duct, keeping the field bloodless and anatomically clear.

(*e*) Expose and tie the cystic artery by itself, *not in an indefinite mass, but alone.*

(*f*) When the cystic duct is exposed, it also should be tied individually.

(*g*) Drainage should be established in Morrison's pouch; and if there is no transverse incision, dependent drainage should be secured by a lateral opening opposite the bottom of Morrison's pouch. If there is a right transverse abdominal incision, drain through the external end of the incision (Fig. 46).

(*h*) The abdominal incision should be closed accurately *by interrupted stitches.*

DON'T!

Don't invite difficulties by making too small an incision.

Don't reach blindly down and grasp an indefinite mass of tissue, hoping the common duct is not included.

Don't divide an unknown mass of tissue about the base of the liver with scissors, *only hoping and not knowing* that no harm will be done.

Don't strip the cystic duct and gall-bladder with gauze. This produces shock and devitalizes tissue that must defend itself against infection.

Don't strip the gall-bladder from the liver with gauze, as tears into the liver will be made.

Don't be in doubt as to the exact positions of the end of the gall-bladder and of the beginning of the cystic duct. These may always be disclosed by splitting the gall-bladder down to the cystic duct. If a small portion of the pathologic gall-bladder is left it may cause much later trouble.

Don't drag heavily on either the liver or the gall-bladder.

Don't fail to examine the common duct before proceeding to excise the gall-bladder.

Don't explore the abdomen with infected gloves.

Don't use force in exploring the cystic and common ducts with a probe.

Don't do multiple operations at one séance if the risk is not good.

Don't use a sharp-cutting needle in suturing the liver.

Don't tie the stitches in the abdominal wall tightly.

Don't forget that adhesions of the omentum and intestines are most easily and swiftly and bloodlessly severed by a sharp knife in conjunction with a clear white field.

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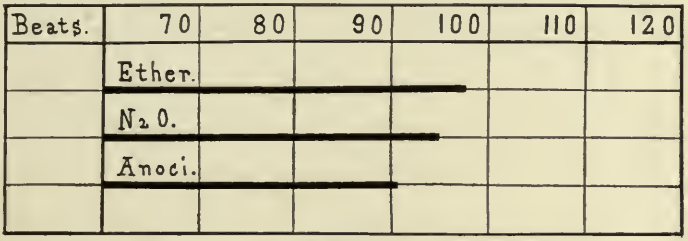


The Pulse.

Each heavy line represents the average 5 P. M. pulse-rate of 10 patients during the first four days after operation.

FIG. 47.—COMPARATIVE CLINICAL RESULTS OF CONSECUTIVE CHOLECYSTOSTOMIES PERFORMED UNDER ETHER ANESTHESIA, UNDER NITROUS OXID-OXYGEN ALONE, AND UNDER COMPLETE ANOCIATION.

Don't use quinin and urea hydrochlorid unless the patient is a bad risk; but *in a bad risk* don't fail to inject large quantities far from the line of incision (Fig. 47).

OPERATIONS ON THE COMMON DUCT

Operations for stone in the common duct, even in the hands of the most experienced and expert operators, yield a considerable mortality rate as compared with operations on the gall-bladder, on the pelvic organs, for exophthalmic goiter, for suppurative appendicitis, etc.

In the common duct operation no vital organ is involved, but merely a duct. Death cannot usually be attributed to the loss of bile or to infection of the peritoneum from bile, but is due to the

gradual development of an asthenic state characterized by dulness of the mental and muscular reactions, a dry tongue, partial suppression of bile, anorexia, scanty urine—together with the impairment of the entire digestive system—a progressive adynamic state which is extremely resistant to any known treatment. Happily not many common duct cases follow this course, but the severity of the postoperative symptoms is in proportion to the difficulty of the technic, which, in turn, depends upon the number of stones and their impactions and the difficulty of discovering even a small stone. One most impressive example of morbid development was in the case of a fairly good risk patient whose entire common duct and a large part of the hepatic duct was impacted solidly with sixty-five stones. The task of extracting these was most difficult, and though the patient went through the operation splendidly, he died on the fifth day with the symptoms above mentioned. Neither infection, nor hemorrhage, nor shock, nor ileus, nor pneumonia, nor urinary suppression were accountable. What then did cause death?

This important question cannot at the moment be correctly answered, but the principal cause of death was quite certainly the trauma of the root of the liver. In common duct cases the liver may be seriously impaired prior to operation. In such a handicapped case the necessary manipulation may damage the liver still more, and as a result its function will be impaired sufficiently to cause death.

The general operative technic is as follows:

Every adhesion is carefully divided by a sharp dissection, which is strictly confined to the white, bloodless line between the peritoneum and the adhesion. No blood-vessel crosses this dead-white line. The whole line of dissection being bloodless, every tissue is accurately identified and little sponging is needed. The stones are laid bare by an ample longitudinal incision through the

duct wall, and are picked out without injuring the duct mucosa. After painstaking exploration of the entire duct lumen the duct is then closed with fine chromic gut on a French needle, just as wounds of the intestine are closed, *provided, of course, that bile drainage through the ampulla or the gall-bladder is assured.* This point is established during the exploration. Drainage of the common duct is required if there has been a stone in the ampulla; if the duct mucosa has been injured so as to cause hemorrhage; if there is probability of postoperative closure of the duct by swelling; and finally, if, in the absence of these circumstances, there still is not a healthy gall-bladder to drain—and usually there is not. If drainage of the duct itself be not required, an iodoform drain is placed near, but not against, the line of sutures. As far as the operation alone is concerned, convalescence should be uneventful.

DON'T!

Don't struggle with an insufficient abdominal exposure.

Don't curet the common duct.

Don't fear to make an adequate longitudinal incision into the common duct.

Don't fail to use the finger as the means of exploration if the duct is greatly enlarged. We have seen the common duct enlarged to the size of the duodenum.

Don't fail to make the transduodenal approach if a stone is solidly impacted in a mass in the ampulla.

Don't forget that if the gall-bladder is pathologically destroyed and the common duct strictured between the entrance of the cystic duct and the ampulla that the duodenum may be mobilized and carried up to the hepatic duct, and the free end of the hepatic duct may be brought into the duodenum and held by sutures. This requires a transverse duodenostomy.

Don't use an uphill drain through the abdominal incision, but

insert the drain through the bottom of Morrison's pouch, closing the abdominal incision with interrupted stitches.

Don't tie the sutures tightly.

Don't fail to give a 5 per cent, sodium bicarbonate solution with 5 per cent. glucose per rectum after operation.

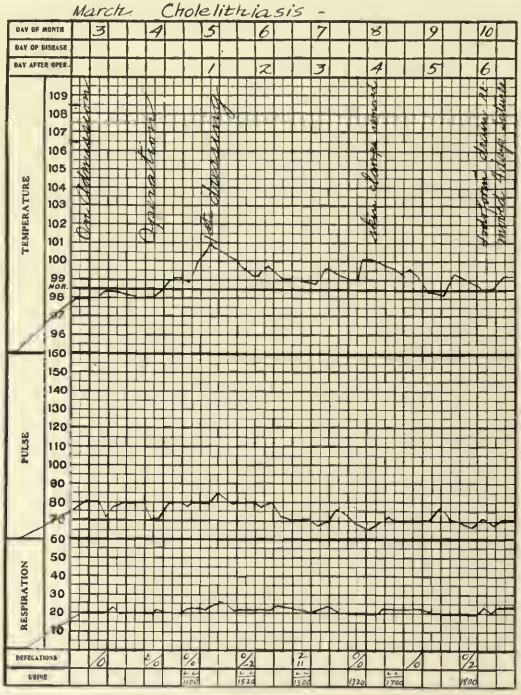


Fig. 48.—Chart Showing the Uneventful Clinical Course after an Operation for Common Duct Stone Performed under *Anociation.*

Don't fail to guard against pulmonary stasis. Turn the patient from side to side.

Don't fail to use massive infiltrations with quinin and urea if the patient is feeble, for the loss of wound pain is a great gain.

Don't use quinin and urea in good risks, because it causes marked local edema.

Don't use any more ether than is demanded—ether and chloroform damage liver cells.

Don't forget to urge much water.

Don't fail to drain the gall-bladder, and to close the common duct tightly, if the gall-bladder can be drained.

Don't operate, if it can be avoided, in the presence of deep jaundice, chills, and high fever.

Don't put drainage in contact with the sutures in the common duct (Fig. 48).

ACUTE CHOLECYSTITIS

Cases of acute cholecystitis usually can be carried over the critical stage into a chronic stage, but when operation becomes necessary, in threatening acute cases, the following plan is strikingly successful:

Under only nitrous oxid-oxygen and with local anesthesia the abdominal wall is divided over the very middle of the most tender, the most rigid area—not where the gall-bladder anatomically ought to be, but where the center of infection is.

The peritoneum is opened most cautiously and an attempt made to divide it wholly and only within the area of adhesion. If adhesions extend down to the distended gall-bladder, they are separated with extreme caution until the gall-bladder wall is reached, so that an aspirating needle may be inserted; the adhesions are separated only sufficiently to meet the absolute requirements for the establishment of drainage. As soon as the gall-bladder is opened (we are now discussing a fulminant acute case) a tube is inserted and nothing more is done surgically. Around this tube a quantity of iodoform gauze is lightly packed, after which large pieces of gauze are inserted around all the sides of the short abdominal incision. No stitches are used provided the incision is short and the gauze packing adequate. As a result the infection collapses, and a rapid convalescence follows. After all the acute

symptoms have subsided, the temperature has remained long normal, and the patient in good condition for a sufficiently long period, then a cholecystectomy is performed.

DON'T!

Don't prolong the operation one moment longer than is absolutely necessary.

Don't try to widen the field of retraction.

Don't manipulate anything.

Don't remove the gall-bladder in the fulminant stage.

Don't be in a hurry to perform a second operation.

Don't use quinin and urea.

Don't hesitate to give morphin.

Don't fail to give much water, especially in the form of a 5 per cent. glucose and 5 per cent. sodium bicarbonate solution per rectum by the Murphy drip.

Don't fail to apply vast moist hot packs over all the dressings.

CHRONIC EMPYEMA OF THE GALL-BLADDER

Chronic empyema of the gall-bladder may cause degenerative changes in the heart, liver, and kidneys. In all cases the gall-bladder should be excised unless some urgent contraindication exists. If the gall-bladder is firmly distended, then aspirate before excising, because the tense gall-bladder may rupture during operation; otherwise conduct the case as an ordinary cholecystectomy.

CHAPTER XII

ANOCIATION IN OPERATIONS ON THE INTESTINES

RESECTION OF THE INTESTINES

GANGRENE resulting from acute intestinal obstruction and the presence of cancer are the two conditions for the relief of which a resection of the intestines is most frequently indicated. Whatever the condition, the first step is an exploration for the purpose of planning the operation and developing the operative field.

First an ample abdominal incision is made under complete local blocking with novocain for whatever condition may be found. The muscles of the abdominal wall will then be relaxed; the exploration will be facilitated; and the use of gauze pads will be reduced to a minimum.

The preliminary exploration will invariably cause a certain amount of trauma in the unblocked territory, especially in the presence of intestinal obstruction. In such a case enough ether should be added to the nitrous oxid-oxygen to ensure sufficient relaxation until the completion of the exploration and of the development of the operative field. If the general condition is poor, then a two-stage operation may be required. When resection of the colon is indicated Moynihan's plan of dividing the peritoneal attachment is most useful, as this mobilizes the colon to a great degree, and permits easy handling with minimum manipulation.

The following are especially important points to be observed in making a resection of the intestines:

1. Use silk sutures.
2. Use round needles.

3. If there is plenty of room, close the divided ends and make a lateral anastomosis.

4. The second choice is end-to-side anastomosis.

5. The last choice is end-to-end anastomosis.

6. If anatomically feasible, protect the suture line with omentum.

7. In very grave cases perform the operation in two stages. In the first stage merely bring out the tumor, cut it away between the clamps, and establish a lateral anastomosis by inserting forceps in each end; complete the operation in a second stage after physiologic balance has been established.

8. Relief from obstruction is the first consideration.

9. The newer methods of controlling infection will minimize that danger.

HERNIOTOMY

In herniotomy, as in all operations under *anociation,* every division of tissue supplied with noci-ceptors is preceded by the infiltration of the part with novocain. The field of operation is kept free from blood by securing the few blood-vessels in the skin and subcutaneous tissues. The white glistening fascia has no blood-vessels, and its parallel strands may, therefore, be bloodlessly divided with a sharp knife. The under surface of the fascia has no vessels running through it at right angles, and the sharp-knife, bloodless dissection is, therefore, carried down to the glistening border of Poupart's ligament. In like manner the inner fascia is bloodlessly divided. The sac, hernia, and cord are thus exposed, and appear bloodless and translucent, but the bloodless dissection does not stop here even if the sac is old and has for a long time been irritated by a truss. The sac is picked up with forceps and is freed for a short distance with a sharp knife. It is then opened between two small Halstead hemostats and the forefinger is introduced, the sac being stretched over it like the finger of a glove. The true peritoneum contains no blood-vessels,

hence there is a white, bloodless line between it and its neighbors. Therefore, no matter how old, how large, or how adherent the sac may be, the knife can be passed all the way around it along this bloodless line. The blood-vessels are the key to this bloodless line of fusion between the sac and its environment, and the presence of the smallest blood-vessel will mean that some extraperitoneal tissue is still adherent to the sac. After dissection is well started the separation of the sac well within the internal ring will be easily accomplished if the assistant keeps the tissue taut by tension with small forceps. Not a single vessel below the subcutaneous veins needs to be tied; and the cord is not handled at all, the sac being sharply and precisely cut free from it.

By this technic the sac is completely excised; the cord is uninjured; the testicle does not suffer at all, and no postoperative suspensory support will be required. As a result of the bloodless dissection the pillars are clearly visible, and their strength and value can be accurately estimated, so that intelligent use may be made of them in the repair.

The procedures we have described apply particularly to operations for the radical cure of inguinal hernia, but in umbilical and postoperative hernia the need for sharp bloodless dissection is equally clear.

DON'T!

Don't tie sutures tightly; tight sutures become loose by cutting; loose sutures become tight by tissue swelling.

Don't use blunt dissection; don't use gauze dissection; use only surgical instruments.

Don't cut doubtful tissue; it may include the vas.

Don't drag on the cord needlessly during operation.

Don't fail to keep a constantly clear surgical field.

Don't include any tissue but fat and muscle in closing the hernia.

RECTAL OPERATIONS

In rectal operations one has a splendid opportunity to test the value of novocain infiltration. The divulsion of the sphincter ani causes strong reflex action; in particular it causes deep inspiration, and thus momentarily disturbs the established rate of inhalation of the anesthetic. In collapse from any cause it is a classic procedure to make use of the vitalizing effect of sphincter dilation. If, however, novocain be infiltrated into the soft tissues around the anus, and the infiltrated area be then subjected to momentary pressure, then, under nitrous oxid-oxygen alone, the sphincter may be completely divulsed without any noticeable reaction.

Postoperative discomfort is an almost invariable sequel to anal and rectal operation, especially when an anal tube is worn. This may be greatly diminished if the entire anal zone be blocked by quinin and urea hydrochlorid in 1 : 600 solution injected *at a safe distance*. Bloodgood states that the results of quinin and urea infiltration "in its elimination of postoperative pain are seen chiefly in rectal work."

CHAPTER XIII

ANOCIATION IN OPERATIONS FOR CANCER OF THE RECTUM AND COLON

Resection of the rectum and lower colon has always been and is still a formidable operation; nevertheless, as is shown by our records, the mortality has been reduced 50 per cent., not by less radical procedures, but as a result of improved methods, even with a more radical operation.

Analysis of the Factors of Danger.—(*a*) Cancer originates chemical poisons which impair the body as a whole.

(*b*) If a partial obstruction exists, it interferes with metabolism (1) by the absorption of the intestinal toxins; (2) by interference with digestion—*i. e.*, with bodily vigor.

(*c*) A frequent source of danger is anemia from occult or frank hemorrhage, and from the hemolytic action of the cancer.

(*d*) Usually the patient has been the subject of a devastating worry.

(*e*) As a rule cancer does not attack the young adult, but occurs rather at the period of life when the normal wear and tear has taken from the patient some of the elements of safety.

(*f*) Postoperative infection is an ever-present danger.

The Plan of Attack.—While we cannot turn back the wheels of time nor counteract the chemical poisons of the cancer, nor give an antidote for the ravages of worry and the damage of fear, we can replace lost blood; we can increase the nutritional balance; we can improve the intracellular metabolism; and we can minimize those factors in the operation which have the same effect on the

brain cells as cancer toxins, as intestinal toxins, as worry, as anemia. That is, we can avoid traumatic shock; we can avoid needless pulling on the intestines; we can avoid hemorrhage; we can avoid needless irritation of the peritoneum; we can minimize the gloomy outlook of the patient; we can avoid postoperative infection in certain cases by a two-stage operation; we can avoid the dread of the second séance by making the first one relatively comfortable. By adapting our methods to meet these factors of demonstrated importance we have been able to make the great reduction in our mortality rate.

Cancer of the Rectum.—For the patient with cancer of the rectum the paramount question or at least the question next in urgency to the possibility of a permanent cure is: Where shall the artificial anus be placed?

We have tried many plans, and have concluded that the Littlewood or high lateral position is perhaps the best, since this provides accessibility and a good opportunity for control.

The two-stage operation is performed in all cases in which an artificial anus is to be made. In the first operation under anociation, the incision is so placed as to allow complete information regarding the local extent and also the dissemination of the cancer to other parts, especially to the liver. If the case is operable, a Littlewood artificial anus is made, and the operative field is surrounded with gauze lightly impregnated with iodoform. These procedures involve a light and a short operation. After the physiologic action of the artificial anus is established and the patient's condition is satisfactory, usually within four days, then the excision of the cancer is made. Since the first operation, usually under analgesia, has caused but little disturbance, the patient looks forward to the second with relative equanimity.

The surgeon, too, may anticipate the second stage with equa-

nimity because of the many safeguards he is able to offer, principal among which are the following:

1. The gauze packing, which mobiizes a strong defense against infection.

2. The improved methods of combating infection and promoting the healing of wounds which have been evolved in war surgery.

3. The control of shock.

4. The established, functioning anus, by which the new wound is completely protected from feces.

5. The continued, unhampered nutrition.

6. The resort to blood transfusion if anemia, or exhaustion, or hemorrhage wears down too much the resistance of the patient.

7. The promotion of the welfare of these cases of tardy repair by a dietetic and hygienic regimen similar to that for tuberculosis —forced feeding and fresh air in abundance.

Artificial Anus.—There has probably never been a better and more practical plan presented for the management of artificial anus than that described by Dr. W. W. Keen, as follows:[1]

"In my later operations I have always made a preliminary colostomy by Maydl's method. At the end of about a week I have excised all of the protruding portion of the bowel, leaving a permanent artificial anus. The advantages of this are, first, that before the operation one can empty the upper bowel completely, and disinfect the lower bowel partly through the natural and partly through the artificial anus. In the paper already alluded to[2] I have shown the impossibility of disinfecting or even of unloading the bowel prior to amputation of the rectum, even after days or weeks of effort. An abdominal artificial anus is very much more under control, and can be cleansed very much better than a sacral anus. One can wear a belt or girdle as tight as is necessary, both to prevent undue protrusion and to prevent the escape of

[1] Journal of the American Medical Association, August 13, 1898.

[2] Therapeutic Gazette, 1897.

the feces. Most of the cases with such an artificial anus have the bowel emptied spontaneously once or, more commonly, twice a day, and at almost as regular hours as by the normal rectum. Of course when there is diarrhea no control over the evacuation remains, but by means of a suitable dressing the contents of the colon, as they escape, are caught and are prevented from becoming a source of annoyance to the patient or those about him.

"In the last two cases upon which I have operated I have taken a further step which I think is a distinct improvement in rectal surgery, namely: after amputation of the rectum I have completely closed the sacral end of the rectum, just as one closes the end of the intestine before making a lateral anastomosis. The first advantage of this is that if the closure is a success, neither fecal matter nor infected mucus can reach the wound, and we are much more likely to obtain primary union, which greatly lessens the danger to life. Second, as the perineal wound is entirely closed, no escape of either feces or mucus occurs after recovery and the patient is relieved of the necessity of wearing a napkin. Third, for the same reasons, we avoid any prolapse."

RESECTION OF THE SIGMOID WITH PRESERVATION OF THE SPHINCTER ANI

If the risk is not good, resection of the sigmoid is preceded by a Littlewood colostomy. The advantages of the two-stage operation in these cases are: (*a*) the greater certainty with which the intestinal anastomosis will heal properly when no feces pass over it as compared with those cases in which during the period of healing the anastomosis is continually irritated by the passage of gas and feces; (*b*) when a functioning artificial anus has been established in advance of the anastomosis, nutrition need not be interrupted. If there is no previous colostomy, unless the sutures hold, all is lost; and in the absence of an artificial anus, physiologic rest is demanded if the sutures are to have their greatest chance of holding. Physiologic rest means not only the withholding of food but also the binding of the bowels. Therefore

auto-intoxication is added to starvation, and both are added to the burden of an extremely grave operation.

SPECIAL TECHNICAL POINTS

In addition to the general plans which contribute to the broader welfare of the patient, as outlined above, the following special technical points may be mentioned:

1. Utilize Moynihan's method for freeing the peritoneal attachment along the external border of the colon; this frees and mobilizes the colon remarkably.

2. Always separate the tissue that holds the colon by sharp dissection, avoiding the blood-vessels.

3. Catch and tie the large blood-vessels.

4. These precautions will obviate any necessity for damaging dragging and pulling manipulations.

5. In suturing, make assurance doubly sure by using the cobbler stitch; this provides not only a hemostatic and fluid-tight union, but also it is the strongest stitch known (see Fig. 45).

6. If there is plenty of omentum, cover the suture line with it.

7. In dividing the intestine, use the cautery as far as possible.

DON'T!

Don't perform multiple operations at one séance, but rather "divide and conquer."

Don't make end-to-end anastomoses in the large intestine unless there is no opportunity for lateral or end-to-side anastomoses.

Don't use cutting needles.

Don't leave stitches under tension.

Don't tie stitches too tightly—they will cut.

Don't explore after making the resection.

Don't do dressings in a painful manner. The early dressings of a Kraske may well be done under analgesia.

Don't fail to pass the hand over the liver *after* finding that the growth in the colon is locally removable.

Don't think of the liver or any other part of the abdomen if the cancer is locally inoperable. Consider only the patient. *Purely pathologic observations are reserved for the pathologist.*

Don't forget that postoperative pain and distress is in proportion to the injury to the peritoneum.

CHAPTER XIV

ANOCIATION IN GYNECOLOGIC OPERATIONS

The removal of benign tumors, except those wedged in the pelvis, may be accomplished under complete *anociation* as follows: The tumor is fully exposed through an ample incision in the novocainized abdominal wall. As the opening has been made under anociation, no traumatic impulse has reached the brain, and the muscles are, therefore, relaxed, so that almost no retraction will be required; and no gauze pads will be required to prevent the expulsion of the intestines, which the force of gravity will hold within the abdomen.

If the tumor is ovarian and is large and if there are adhesions in the accessible field, these are divided within the narrow, white bloodless line on the peritoneal surface of the tumor by a knife with a keen edge. However old or firm the adhesion may be, no blood-vessel will cross this dead-white line. This line of division may be kept straight and its breadth increased if an assistant make steady tension with a large piece of gauze. This tension need not—*must not*—be sufficient to excite nocuous impulses, but should be sufficient to facilitate the sharp division of this white line of fusion between the tumor and the parietal or intestinal peritoneum. This feather-edge division can be made in a much shorter time than can a rough bloody separation, especially since it eliminates the time required by the latter method for hemostasis. It is surprising to what a depth the sharp dissection may be carried within the pelvis. Even beyond the reach of the knife, however, the advantage of this technic becomes obvious, for the exact cleavage line being established, as a rule,

the remainder of the tumor—bluntly, but with *finesse*—may readily be separated with the wet gloved hand.

The principle of anociation obviously demands that the body of the tumor itself shall not be delivered by assault, but by strategy —by coaxing pressure and lifting. Almost any tumor, except those molded into the pelvis in the course of their growth, can be delivered without tightening of the abdominal muscles, without disturbing the even curve of the respiratory excursion.

Clamp compression alone, without novocainization, would cause relatively slight response. The common error at this point, in the language of golf, is that of "pressing"; that is, the operator is so anxious to get the tumor out that he handles it needlessly and harmfully. As a consequence, the patient awakes locally and makes a mute but serious protest against the injury.

The authors have never seen any evidence of nociceptors for sharp-knife cutting in the body of a tumor or in the normal uterus. The principal thing to avoid is too much pulling.

In a hysterectomy one is apt to suture too much tissue and to tie it too tightly. Ochsner long ago called attention to this point, and Bartlett has shown that precision in vascular control requires that accurate attention be given to the main vascular trunks, after which the remainder of the wound may be closed as one closes an external wound.

John G. Clark demonstrated how practical vascular control without excessive suturing may be secured in myomectomy. In this phase of the operation the surgical rule, that gentle accuracy should be employed rather than needless force, is especially applicable.

By means of Kelly's curved needle, Franklin Martin's long dissecting forceps, the Andrews needle-holder, and long flexible retractors any part of the pelvis may be sutured with accuracy and dispatch in the field relaxed under *anociation*.

In cases of chronic gonorrheal salpingitis, with or without tubal abscess, sharp-knife dissection gives ready access to the precise cleavage line. Beginning at the most accessible point, the adhesions are divided as far as possible by sharp dissection. The adhesions may be so thick and their fusion with the intestinal coils so firm as to occasion a good deal of difficulty, but usually at some point the tubo-intestinal cleavage line will be reached, after which the separation will be readily made.

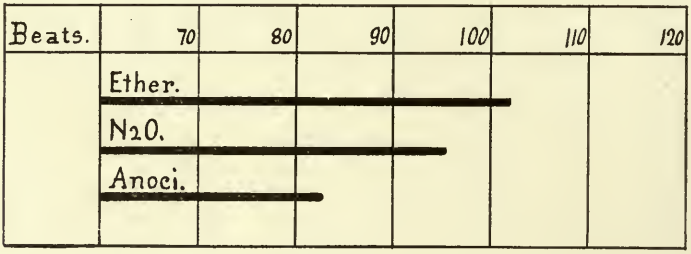
By *anociation* one may deal readily even with those cases in which the fundus uteri is well up in the pelvis, the proximal end of the tube being thickened, but not seriously involved, while at the distal end the fimbriated extremity has grasped the ovary and is pouring into it its infection, causing tubo-ovarian abscess.

With a sharp knife the diseased tube is freed from the uterus by means of a V-shaped cut, the bleeding points being caught with a Kelly needle and plain catgut in an interlocking suture lightly tied. The tube extends down into the pelvis like an inverted pyramid; its attachments may be divided with ease, and finally the pus tube may be lifted out.

In case of a double tubo-ovarian abscess a part of one or of both ovaries and any uninfected portion of the ovarian attachments are preserved. Division of the ovary does not cause the slightest pain.

If the uterus be down in the pelvis, with the tubes and ovaries above it, it will be found that the abscesses extend well downward toward the fundus uteri. In such a case the ovaries usually fare better and the uterus worse. The latter may be enlarged, edematous, heavy, and infected. In many such cases it is necessary to remove a portion of the uterus and the tubes *en masse*. Here *anociation* is best attained by taking the operation to the field rather than by dragging the organs up to the level most convenient for the surgeon. In an adequate, relaxed field, by strategic maneuvers,

the uterus and tubes may be divided by a sharp knife—the sharp-knife division causing not a single break in the respiratory rhythm.



The Pulse.

Each heavy line represents the average 5 P. M. pulse-rate of 10 patients duing the first four days after operation.

FIG. 49.—COMPARATIVE CLINICAL RESULTS OF CONSECUTIVE ABDOMINAL HYSTERECTOMIES PERFORMED UNDER ETHER ANESTHESIA, UNDER NITROUS OXID-OXYGEN ALONE, AND UNDER COMPLETE *Anociation*.

In the Coffey operation for suspension of the uterus, which we usually employ, the broad and the round ligaments may in certain cases be blocked (Fig. 49).

CHAPTER XV

ANOCIATION IN GENITO-URINARY OPERATIONS

The principles described in their relation to operations upon other organs apply with especial force to operations upon the urogenital organs, and genito-urinary operations under *anociation* show markedly better results than those performed without this protection.

BLADDER

The urinary bladder is an extremely sensitive organ, and if it is excessively or roughly handled, marked shock is produced. In many of the conditions of this organ which necessitate surgical intervention, such as the presence of foreign bodies, tumors, diverticula, etc., there is nearly always an accompanying infection of the entire urinary tract, with reduced functional activity of the kidneys. Therefore, the greatest care must be taken not to add to the handicap of these patients by an improper operative procedure. Moreover, pathologic conditions of the urinary bladder often occur in persons past middle life, whose ability to withstand traumatism has been reduced. In many cases, also, the local condition is of long standing, and the patient is much exhausted from the prolonged suffering and irritation.

In operations upon the bladder the first step is to cleanse the bladder thoroughly with a mild antiseptic. If the bladder is very sensitive a solution of 1 per cent. alypin or of 2 per cent. novocain is introduced through a catheter, the solution being retained in the bladder by clamping the catheter. Then, under nitrous oxid-oxygen anesthesia, the skin, subcutaneous tissues,

and muscles are infiltrated with novocain (Fig. 50). After the incision has been made the bladder is brought up into the wound by gentle traction with a pair of bladder hooks, and the line of incision through the bladder wall is completely blocked (Fig. 51). The bladder is then emptied by releasing the clamp on the catheter. The combination of the infiltration of the bladder wall, with the preoperative injection of alypin or novocain, will so completely anesthetize all areas of the bladder that the manipulations of operations for stone, for tumor, or even for diverticula may be carried through without the slightest nerve-muscular response on the part of the patient.

PROSTATE

An especially urgent indication for the application of the principles of *anociation* is presented by the patient for whose relief a prostatectomy is required. These patients generally present the combination of old age, infection, diseased kidneys, weakened heart and blood-vessels, and the usual depletion of resistance which must result from such a combination. In other words, these patients are extremely handicapped. Yet in no series of patients has the percentage of improved results under *anociation* been proportionately greater than among these.

The special sources of danger in prostatectomy are the anesthetic, shock, and hemorrhage. As a result of many efforts to diminish these dangers the following method has been evolved by means of which the operation may be performed without hesitancy upon such patients as are described above, who, because of their age or because of diminished vitality, have been considered bad operative risks. Patients who undergo a prostatectomy performed by this technic are not only free from shock, but are in splendid condition after the operation to combat any other untoward influence that may arise during convalescence.

FIG. 50.—BLADDER OPERATIONS: INFILTRATION OF SKIN WITH NOVOCAIN.

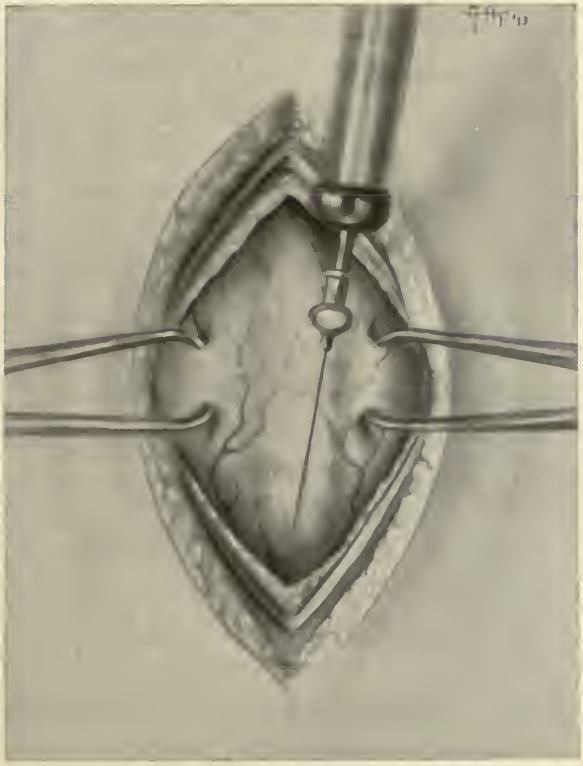


FIG. 51.—BLADDER OPERATIONS: INFILTRATION OF BLADDER WALL BEFORE OPENING.

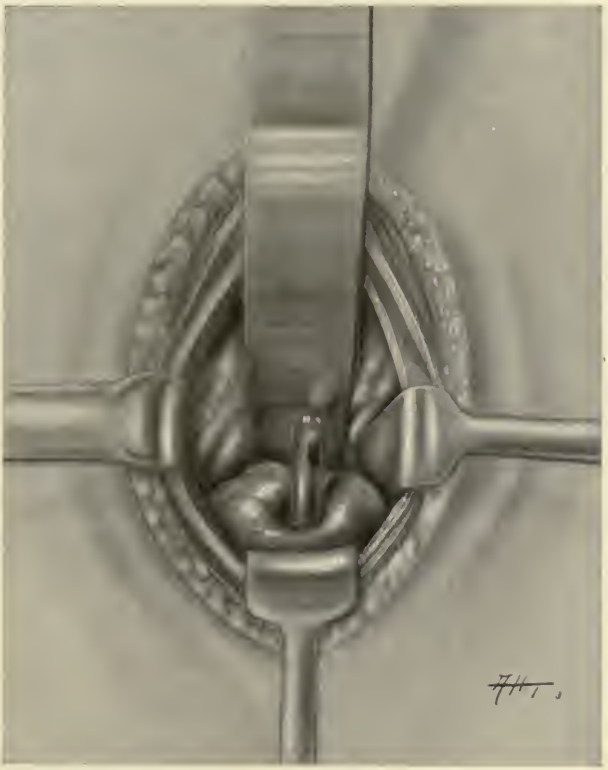


FIG. 52.—PROSTATECTOMY: INTRAVESICAL EXPOSURE OF THE PROSTATE.

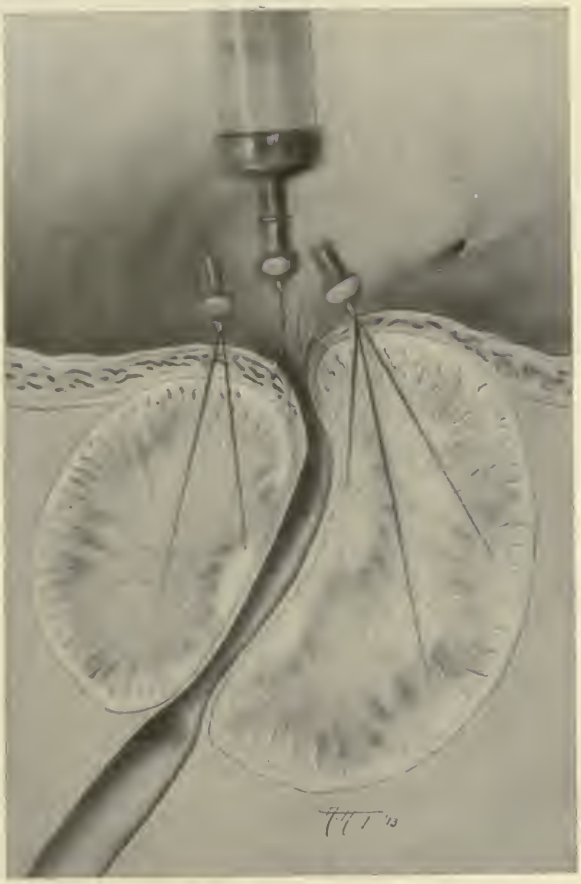


FIG. 53.—PROSTATECTOMY: INFILTRATION OF CAPSULE OF PROSTATE BEFORE REMOVAL.

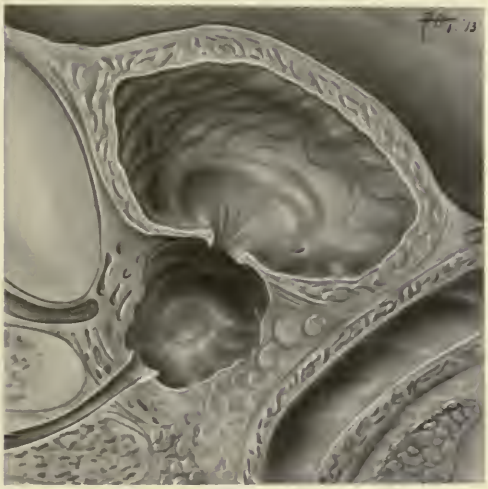


FIG. 54.—PROSTATECTOMY: CAVITY LEFT AFTER ENUCLEATION OF THE PROSTATE.

FIG. 55.—PROSTATECTOMY: GAUZE PACKING BY WHICH THE RAW SURFACES OF THE CAPSULE ARE BROUGHT IN APPOSITION.

As in bladder operations, the preliminary dose of morphin and scopolamin is followed by the injection through a catheter into the bladder of 60 or 90 c.c. of a solution of 1 per cent. alypin or 2 per cent. novocain. The catheter is clamped and allowed to remain. The technic described for bladder operations is followed until the prostate is exposed intravesically (Fig. 52). The bladder mucosa of the projecting prostate is infiltrated with novocain, and a deep infiltration is made along the edge of the capsule (Fig. 53). *With careful and most gentle manipulations the prostate is enucleated with the finger* (Fig. 54). Not *"how rapidly,"* but *"how carefully"* is the slogan. Narrow strips of gauze are packed around the catheter above the mucous membrane so that the raw surfaces of the capsule are brought in apposition—a procedure which effectively prevents hemorrhage (Fig. 55). The two ends of the urethra also are brought closely together by this means, so that a continuous funnel-shaped mucous membrane results—a most important factor.

At the close of the operation the color of the patient will be good; the pulse and respiration will not be increased; in fact, may be even lower than before the operation. The patient will rest comfortably, will be free from nausea, can take water easily, and a speedy, uninterrupted convalescence may be anticipated.

KIDNEY

The approach to the kidney is through tissues which, in their evolutionary development, have not been subjected to environmental trauma; consequently they are not so richly endowed with nociceptors as are the tissues of the anterior abdominal wall. There are, however, a sufficient number of nociceptors in the skin and muscles to make their infiltration advisable.

Parts of a kidney operation in which the *anoci* technic is ur-

gently demanded, however, are the separation of the adherent kidney from its attachments and its delivery into the wound.

The first and most important requirement in an operation upon the kidney is an *ample incision*. An ample incision with the muscular relaxation obtained through *anociation* makes clearly visible the lines of adhesion. The adhesions should be divided by sharp dissection until the line of cleavage is reached. In the case of a suppurating kidney the line of easy cleavage is on the posterior surface of the kidney itself underneath the thickened capsule. In a tuberculous kidney, however, the separation must be made outside the capsule in order that the wound may not be infected with tubercle bacilli. Old tuberculous kidneys present dense and strong adhesions, most of which, however, may be readily divided by sharp-knife dissection.

The easier kidney operations on good risk subjects are relatively safe by even the most nocuous technic; but the protection of *anociation* is urgently needed by the patient reduced by hemorrhage or infection, or by a patient the functional power of whose kidney has been perilously reduced by any cause.

GENERAL POINTS TO BE OBSERVED IN GENITO-URINARY OPERATIONS

1. Always use nitrous oxid-oxygen as the inhalation anesthetic.
2. Make ample incisions to avoid traction.
3. Use local anesthesia freely in bladder operations.
4. Close bladder by sutures whenever possible except in prostatectomies.
5. When possible, drain bladder through an in-lying catheter.
6. Keep patients in sitting position in bed as much as possible after operation.
7. Give plenty of fluids, fresh air, and nourishing food.
8. Always consider the patient as a whole, and not his local lesion only.

DON'T!

Don't operate against time; one minute of rough handling may kill the patient.

Don't divide renal vessels before they are securely clamped.

Don't wait, if there be much oozing, to see if the patient will be affected by it; when that stage has been demonstrated, it will generally be too late for remedy.

Don't operate on the genito-urinary tract before the kidney function has been demonstrated.

CHAPTER XVI

ANOCIATION IN THE TREATMENT OF EXOPHTHALMIC GOITER

Every one will agree that a technic that can carry a case of advanced exophthalmic goiter through an operation without increasing the pulse-rate can all the more readily do as much in any other operation. It was in large measure the study of the preoperative and postoperative course of cases of exophthalmic goiter which led to the development of the shockless operation in general surgery.

A searching inquiry into the past history of a patient with exophthalmic goiter will frequently elicit the fact that he has undergone some emotional experience, often so deeply disturbing in its nature that it has become a dominant emotional stimulant, absorbing attention during the day and disturbing sleep at night. The constant recurrence of this damaging stimulus is attended by an increase of all the emotional phenomena, so that gradually a state is reached in which the effects of the constantly present stimulus remain unchanged. The eyes protrude; the body trembles; the facies of anxiety is present; the thyroid is permanently enlarged; the entire emotional mechanism is involved (Fig. 56).

In such a state any excitation which might produce slight apprehension in a normal individual becomes an overwhelming stimulus. In patients with exophthalmic goiter the mere proposal that an operation be performed becomes a pathologic excitation which may so increase the disease that the patient is even less able than before to make up his mind to submit to adequate treatment. On all sides the patient is beset by vicious circles,

FIG. 56.—TYPICAL CASE OF EXOPHTHALMIC GOITER SHOWING CHARACTERISTIC FACIES.

by pathologic interactions. The ideal plan of approach, therefore, is to assure the patient that his malady is curable; that treatment can best be administered in a hospital; that non-operative measures will first be tried, but that if they prove inadequate, a simple operation will be performed; that it will be best to leave the final decision as to the advisability of an operation to the medical adviser; and that, since even the discussion of an operation is both unpleasant and injurious, it will be best not to open the subject again.

If the patient, as is usually the case, consents to leave the whole matter to the judgment of the physician, the way is opened for the most effective treatment which in our judgment has ever been proposed for exophthalmic goiter; that is, ligation or excision under the protection of *anociation.*

For several days the anesthetist with the paraphernalia for the administration of nitrous oxid-oxygen administers to the patient "inhalation treatments." On the morning of the operation, which is performed in one of the favorable cycles of the disease, the hypodermic injection contains morphin and scopolamin; nitrous oxid is added to the oxygen "inhalation," and the patient falls asleep in bed without realizing that the first step in the operation is being taken. The anesthetized patient is transported to the operating-room, where the operative field is prepared. In the operation itself each division of tissue is preceded by the infiltration of novocain (Figs. 57, 58), and sharp dissection and gentle manipulations are employed throughout. In grave cases quinin and urea hydrochlorid may be injected into every part of the operative field before the wound is closed, though the need for this protection may be neutralized by the employment of a technic so gentle and strategic that a minimum amount of trauma is caused.

The patient is kept under anesthesia until he has returned to his room, which has been restored to its condition when the ad-

ministration of the anesthetic was started. In the course of the cycle from his room to the operating-room and to his return the patient's brain has received no activating stimuli, and no record of the operation has been written upon either the conscious or the subconscious brain.

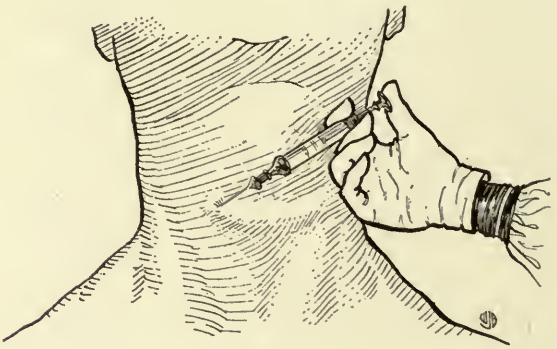


FIG. 57.—THYROIDECTOMY: INFILTRATION OF SKIN.

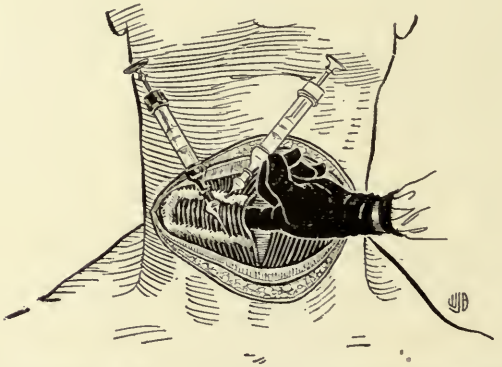


FIG. 58.—THYROIDECTOMY: INFILTRATION OF MUSCLE BEFORE DIVISION.

By this technic the scope of the operation is greatly increased, and the thyroid can be resected in any patient whose condition can endure the metabolic influence of the withdrawal of so much active gland tissue. In cases in which the excision of a lobe is contraindicated it is best to ligate one or both poles, ex-

cising the lobe later, if it is necessary. Ligation is performed without removing the patient from his bed. Nitrous oxid-oxygen may or may not be administered, but the brain is always protected by a complete novocain infiltration.

As for the technic of the excision itself the transverse incision should be sufficiently ample to expose the gland to its lateral border (Fig. 58). The important part of the dissection may thus be in full view without more than nominal retraction of the muscle. The operation should be so bloodless throughout that the lymphatic vessels can be everywhere seen and identified. This may

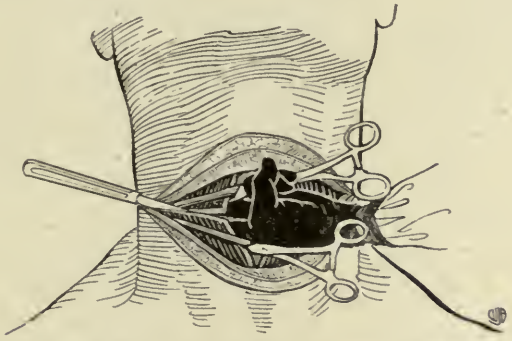
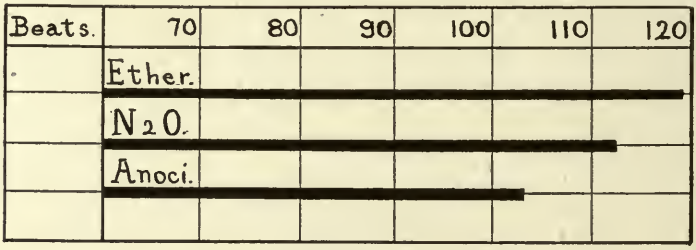


FIG. 59.—THYROIDECTOMY: BLOODLESS DIVISION OF MUSCLES BETWEEN CLAMPS.

be accomplished if *every blood-vessel is divided between clamps* (Fig. 59). The field will then always be completely visible, and being thus controlled, the dissection is carried entirely *on the capsule itself* to the point at which the gland is to be divided. We follow the plan of C. H. Mayo in leaving a small margin of gland adjacent to the larynx. The hoarse voice which used to be a frequent sequel to thyroidectomy has been largely eliminated by *always picking up tissue parallel to the larynx and trachea, and never at right angles to them.* If the Halsted forceps are applied parallel with and closely against the capsule of the gently retracted

gland, no paralysis of the vocal cord will follow, while the parathyroid will rarely if ever be endangered, nor will its blood-supply be disturbed.

The surgeon also must protect *himself* from a certain psychic phase which is apt to develop in difficult goiter operations, and which corresponds to the "break" of the pointer dog when he "rushes the covey." As the surgeon follows a trying and teasing path around a baffling lower border where now and then a small vein is opened and momentarily veils the field, he will again and again be tempted to rush the operation, thus losing his technical



The Pulse.

Each heavy line represents the average 5 P. M. pulse-rate of 10 patients during the first four days after operation.

FIG. 60.—COMPARATIVE CLINICAL RESULTS OF CONSECUTIVE THYROIDECTOMIES PERFORMED UNDER ETHER, UNDER NITROUS OXID-OXYGEN ALONE, AND UNDER COMPLETE *Anociation.*

control of the field. To yield to this temptation is to court trouble.

The benefits of the operation do not end with the immediate results. The postoperative reaction is prevented or minimized, and the later clinical results are relatively as much improved as is the immediate postoperative condition (Figs. 60, 61).

The evolution in our clinic of the described plan for the surgical treatment of exophthalmic goiter—the trials and errors with their narrow escapes, the progress and the unexpected failures, the hopes and the disappointments, the constant search in the

FIG. 61.—A STRIKING ILLUSTRATION OF THE END-RESULTS OF THE SURGICAL TREATMENT OF AN EXTREME CASE OF EXOPHTHALMIC GOITER.

laboratory for help, the search for analogies in other diseases and operations—may be summed up in the following brief account:

In our first experience with operations for exophthalmic goiter, performed according to routine methods, which included the transportation of the *conscious* patient to the operating-room, ether anesthesia, no protecting local anesthesia, a violent reaction always occurred as the day and hour of the operation approached, which was augmented by the transportation to the operating-room and the administration of the anesthetic, and continued throughout the operation and far into the postoperative period. All these unfavorable factors yielded a forbidding mortality. At that time we believed Kocher's dictum, that the violent reaction was due to the absorption of thyroid secretion. Every preventive device was tried, we even kept the wound open and packed with gauze; we cauterized the raw surfaces; but the results were not improved.

One day a patient became delirious on her arrival in the anesthetizing room. She was returned to her room without operation, but a typical violent reaction, the so-called "hyperthyroidism," developed. Her temperature rose to 109° F., her pulse to over 200 before her death, which occurred in six hours. This experience and the commonly noted strong resemblance of the gross phenomena of so-called "hyperthyroidism" to the phenomena of fear suggested the following question: If this violent reaction, which was identical with those following operation, was a "hyperthyroidism," then was the increased thyroid secretion in this unfortunate patient caused by fear? To find an answer we undertook an experimental research on fear in animals in which we found that fear produced the characteristic changes of activation and exhaustion in the cells of the brain, the liver, and the adrenals. If, as these results suggested, the "hyperthyroidism" was caused by fear, then the avoidance of fear should at least diminish operative "hyperthyroidism." We therefore evolved the plan of

"fictitious anesthesia" described above, by which the operation, of course, is performed with the full consent of the patient, but without her knowledge of the exact time.

Our operative results were at once markedly improved, but soon it was evident that the patient under general anesthesia, but without local anesthetic protection, responded to every surgical contact. At about this time we had found in the laboratory that local anesthesia prevented surgical shock. If, as our operative experience indicated, the cause of surgical shock is identical with the cause of so-called postoperative "hyperthyroidism," then the complete blocking of the entire operative field by local anesthesia, thus cutting off the brain from communication with every surgical contact with sensitive tissue, in addition to the complete elimination of fear and worry, should result in an operation free from "hyperthyroidism."

Strikingly good results were secured at once by the application of these conclusions. The elimination of the psychic and the traumatic factors greatly reduced the mortality rate—from about 5 to 1.

We then argued that if exophthalmic goiter is due to excessive thyroid activity and to nothing else, and if enough of the thyroid tissue is removed, then why should there be any mortality? Why should the patient go through the operation unmoved, and then on the second day after show a lively reaction, occasionally even die? Instead of complete control, some adverse factor still remained. The three remaining possible sources of trouble were the *anesthetic, the pain of the wound, and the sudden removal of so much thyroid tissue.*

Wound Pain.—To eliminate the wound pain after the thyroid was removed we blocked the entire wound with quinin and urea hydrochlorid, thus causing a local anesthesia for from four to six days. This resulted in immediate improvement. To be sure,

although the pain was dulled, the neck was uncomfortable and stiff, and the quinin caused a marked edema of the tissue and occasionally interfered with healing. But an edematous wound with decreased comfort was to be preferred to the factor of pain which might contribute to a fatal issue.

What relation has the removal of a gland with as great physiologic power as the thyroid to the delayed reaction? Does its removal result in an unbalanced metabolism? That this is the case became apparent in the postoperative course of patients who underwent a marked reaction on the day after operation in spite of the fact that the operation had been performed under such complete *anociation* that there was not a change in the pulse-beat and no postoperative pain. We are now speaking only of desperate risks, cases that under our former operative technic would never have seen a second day. All ordinary risks made easy recoveries.

It was apparent that a part, at least, of this delayed reaction was due to the too abrupt removal of thyroid tissue. We followed this lead by dividing the operation into multiple stages. We first ligated one artery; then the second, and followed by a period of rest. We then excised a portion of one lobe, and in a final stage the entire opposite lobe. This strategic division of the attack still further improved the results in the desperate cases. In addition, we tried the effect of the administration of thyroid extract from twelve to twenty-four hours before the thyroidectomy. This apparently has contributed to the improved results. We have kept constantly in mind that the surgical problem of exophthalmic goiter must be regarded as unsolved until we can operate safely on every case in which the process of dissolution is not actually in progress at the time of operation.

The Anesthetic.—Coincident with our other investigations we were studying the anesthetic factor. Our researches resulted in the substitution of nitrous oxid-oxygen for ether, with greatly

improved results; but there still remained an unexplained factor in connection with the anesthetic. Our consideration of this problem disclosed a most interesting analogy. Clinical analysis discloses the presence of an acidosis in the state of "hyperthyroidism"—severe acidosis that increases as death approaches. Observation of the likeness of the phenomena of inhalation anesthesia to the phenomena of acidosis suggested the laboratory study of the H-ion concentration of the blood in inhalation anesthesia which has been described in a preceeding chapter. These findings—that acidosis was always present in inhalation anesthesia; that the acidosis produced by ether was more prolonged than that produced by nitrous oxid; that the acidosis was proportionate to the depth of anesthesia; and that when the normal alkali-acid balance was reversed—that is, when the blood lost its alkalinity and became acid—death occurred—betrayed the source of danger in the anesthetic factor in the treatment of this exquisitely sensitive disease. It showed that the acidosis of the anesthetic added to the acidosis of the disease might push the desperate case across the already narrow margin of safety. This meant that in a grave risk the depth and the length of anesthesia must be lessened. We therefore adopted what has proved to be one of the most beneficent as well as one of the most interesting developments in the progress of the surgical treatment of exophthalmic goiter—nitrous oxid-oxygen *analgesia*. Analgesia causes no acidosis whatever. Analgesia is a beatific state in which fear and worry and pain are absent and only a contented consciousness remains. But analgesia can be maintained only by a most skilful grading of nitrous oxid which is incompatible with the moving of the patient from bed to surgical carriage; from room to operating theater. We therefore adopted the policy of taking the operation to the patient instead of bringing the patient to the operation. In these desperate cases we perform the operation

on the patient in bed under analgesia and local anesthesia. In order that the precise state of the analgesia may be known—whether too deep, too shallow, or just right—the patient is leisurely and continuously throughout the operation engaged in conversation by the surgeon, the anesthetist, or another person. By this simple means the anesthetist always knows just where the patient is, and the sole guide to the depth of the analgesia is the intellectual response of the patient.

The patient is not allowed to penetrate beyond nor return from the happy state of analgesia until the operation and the dressings are completed. In a grave risk the entire neck wound is left open for twenty-four hours. This gives entire freedom, prevents stiffness and restraint. The wound is closed on the next or following day under analgesia and heals without difficulty; and, incidentally, it requires no drainage. Following the lead suggested by the fact that with each degree of rise in temperature in a biologic as in a physical system, chemical activity—metabolism—is increased 10 per cent.; and conversely, that with each degree of fall in temperature metabolism is decreased 10 per cent., we have attempted to control the excessive postoperative metabolism, which in some cases of exophthalmic goiter is manifested by an acute rise in temperature shortly after operation by the application of an ice-pack. In these cases the consequent decline of the temperature has been as dramatic as its rise. (See Charts, Fig. 62.)

Thus through many trials and errors and constant analysis and criticism, with the active co-operation of a laboratory devoted to the problems suggested, with a receptive hospital and nursing management, and an especially devoted, untiring staff of surgeons and anesthetists, the present surgical treatment of exophthalmic goiter has been evolved. It represents the most complete *anociation* we have been able to develop. At last we have arrived at the

stage in which we can pleasantly and securely anociate these patients. We have now only an occasional death among these frail and shattered human beings. In fact, our recent records show a series of 206 consecutive thyroidectomies and 87 ligations without a goiter death, the one death in the series being due to double pneumonia.

The exophthalmic goiter patient is exquisitely susceptible to all stimuli. Of special importance are the stimuli of trauma, of

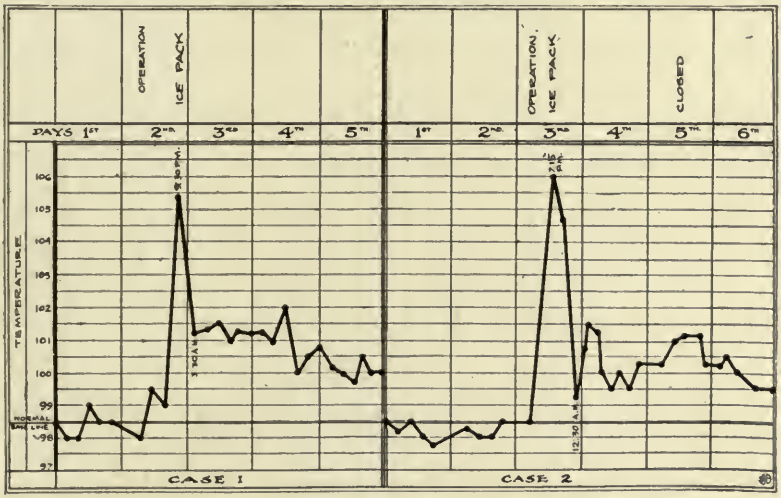


FIG. 62.—EFFECT OF THE APPLICATION OF AN ICE-BAG IN CASES OF EXOPHTHALMIC GOITER, SHOWING AN ACUTE POSTOPERATIVE RISE IN TEMPERATURE.

emotion, of infection. We have spoken of fear and trauma, we must add that infection is especially dangerous. We have seen a case of advanced exophthalmic goiter die from a cold. Even a slight infection causes an exaggerated febrile and general reaction which is analogous to the striking response to slight injury, to slight fear, to slight worry. The various types of defense mechanism whose action requires the transformation of energy are all sensitized.

As to the individual case, it may be treated by one of three general plans which are graded according to the degree of severity of the disease:

1. In moderate cases the entire operation may be completed in one séance. In fact, with the possibilities of control by present methods of *anociation,* it is possible in a large proportion of the cases to perform the whole operation in one stage.

2. Cases of greater severity, but which are fair risks, may require a preliminary ligation, which is always done with the patient in bed under analgesia and local anesthesia. After an interval of from six weeks to two months the lobectomy is done in one séance, as in Group 1.

3. Cases which are on the brink of dissolution may not endure even a ligation at first. In these extreme cases we may first inject into the gland a small quantity of hot water (Porter), repeat after a brief interval, and later ligate first one vessel, then a second vessel. During these maneuvers the patient is kept constantly in bed, and every art is lavished by the nurse and by the staff to ensure quiet and peace. If after the second ligation there is not sufficient improvement to warrant a lobectomy, only a part of a lobe is removed under analgesia and local anesthesia, with the patient in bed. The wound is left open for twenty-four hours and is then closed. After another interval a second larger block of tissue is removed in similar manner, and the patient is sent away with the greater part of the smaller lobe excised to wait under an explicit hygienic regimen until improvement has progressed sufficiently to permit the safe removal of the second and larger lobe. After this final operation there is an onrush of improvement, though final recovery demands that the carefully outlined hygienic regimen be followed for a prolonged period in a care-free, restful environment.

A comparison of the records of the cases of exophthalmic

goiter operated upon at Lakeside Hospital shows in 28 consecutive *ether* cases an average increase of 25 beats in the pulse-rate in the first twenty-four hours after operation and 29.9 beats during the operation; while 28 consecutive *anociated* cases showed an average rise of but 3.03 beats in the first twenty-four hours after operation and a *fall* of *6.39 beats during the operation.*

Our records include 2540 thyroid operations, of which 1171 were for exophthalmic goiter.

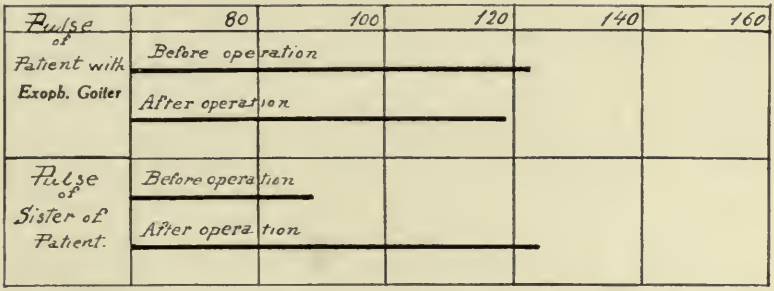


FIG. 63.—CHART ILLUSTRATING PROTECTION AFFORDED BY USE OF *Anociation* IN THYROIDECTOMY.

The patient's brain received neither traumatic nor psychic stimuli from the time she was anesthetized in bed until she returned again from the operating-room. Her pulse-rate *fell* slightly during the operation. On the other hand, the psychic strain undergone by the patient's sister while the operation was being performed caused her pulse-rate to rise to 124.

We feel increasingly secure in our judgment as to when to remove the gland and how much to remove. No problem in surgery has been more interesting—more illuminating. No other disease expresses itself in such dramatic terms. Exophthalmic goiter displays normal processes as if under the magnification of a microscope, and therefore offers an illuminating view of normal as well as of pathologic physiology. Our study of this disease has compelled us to adopt methods and viewpoints that have been of value in many other problems of the operating-room (Fig. 63).

CHAPTER XVII

ANOCIATION IN OPERATIONS FOR CANCER OF THE BREAST

In our series of 1031 operations on the breast we have found that few large operations produce less shock than does an excision of the breast. In certain cases every *anoci* precaution must be taken in this operation, however, because patients with cancer of the breast may be heavily handicapped by long illness, by overwork and worry, by age—by all the noci-associations which accompany this disease, not the least of which is the crushing fear of the cancer itself.

Sharp-knife dissection; the avoidance of blunt dissection, of rough sponging, of sharp-hooked retractors; the protection of the raw surface; adequate exposure of the field in the axilla; the complete control of hemorrhage—all these are sufficient guarantees that there will be no shock.

To minimize postoperative pain and to prevent infection from necrosis of the tissues the skin surfaces should not be pulled together with tight sutures, but to avoid tension the field should either remain open, skin-grafts being made close to the surface, or the Rodman technic for making skin-flaps should be employed.

CHAPTER XVIII

ANOCIATION IN OPERATIONS IN THE MOUTH AND NECK

CANCER OF THE LARYNX

The value of the two-stage operation is perhaps best illustrated by the two-stage operation for cancer of the larynx, in the first stage of which, by means of a preliminary gauze packing, that very vulnerable area, the mediastinum, and the region along the deep vessels and the trachea and esophagus are amply prepared to resist the inevitable exposure to infection when the larynx is removed. This technic eliminates the great danger of mediastinal infection which, after pneumonia, has been the most dangerous result of laryngectomy. The explanation of the characteristic painless, tedious, and fatal course of mediastinal abscess is probably found in the fact that the bony chest wall has always protected this region of the body from wounds. Being protected against wounds through the vast periods of man's evolution, it has been also protected against infection. The tissue of this protected region, therefore, has not been endowed with the defense mechanism required to meet and overcome infection, as have been, for example, the peritoneum and the external parts of the body. In view of this fact we must guard this helpless territory with special care by means of preoperative protection. An ideal defense is made by opening and packing the deep planes of the neck, and at the same séance making a tracheotomy. By this means the mediastinum is put under strong guard, and at the same time the later technic of the laryngectomy is measurably reduced.

The danger of vagitis may be eliminated if the dissection is carried on one side of the larynx all the way to the upper margin of the field of final operation, this territory being packed with iodoform gauze just as the deep planes of the neck are packed (Fig. 64). By this procedure one vagus must take the brunt of

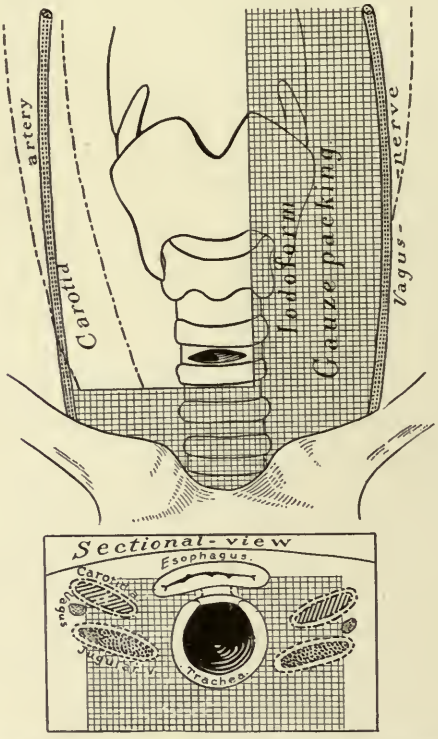


Fig. 64.—Laryngectomy: Schematic Drawing to Illustrate the Method of Packing the Lateral Planes of the Neck with Iodoform Gauze at Preliminary Operation.

exposure and adjustment before the larynx is removed. By the time the laryngectomy is done this vagus will be readjusted and ready to resume its function in case it be affected at all, and so the heavy onslaught of the vagi upon the heart will not be made by both vagi simultaneously.

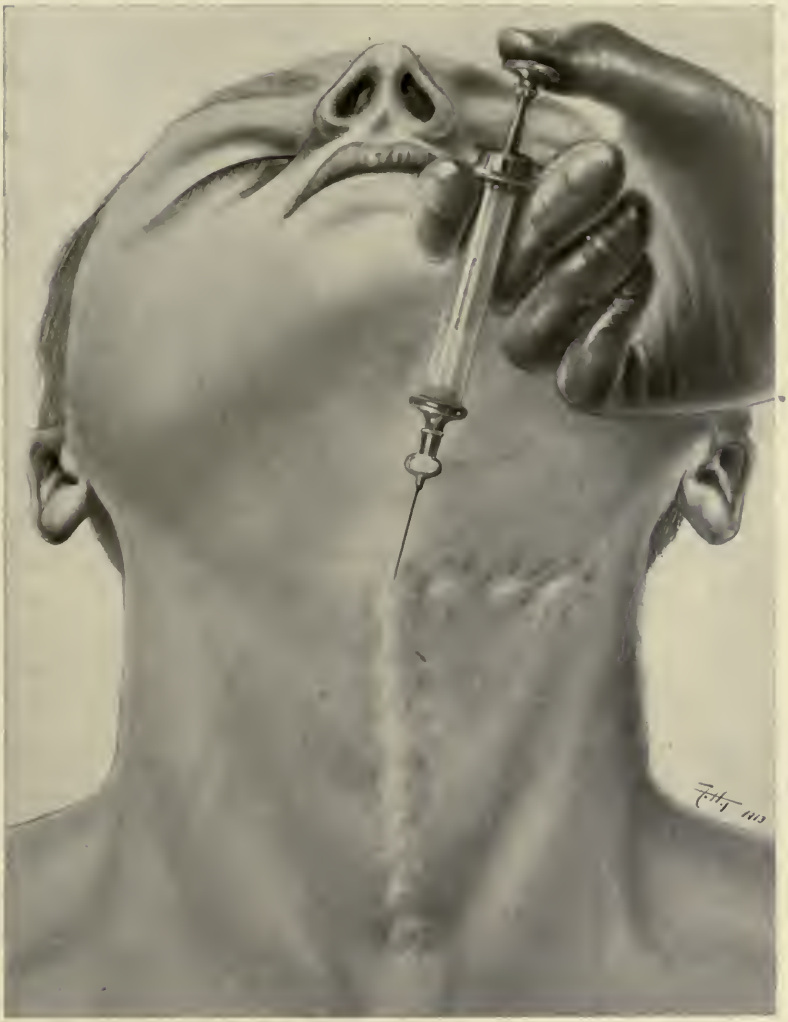


FIG. 65.—LARYNGECTOMY: INFILTRATION OF SKIN WITH NOVOCAIN.

FIG. 66.—LARYNGECTOMY: INFILTRATION OF FASCIA WITH NOVOCAIN.

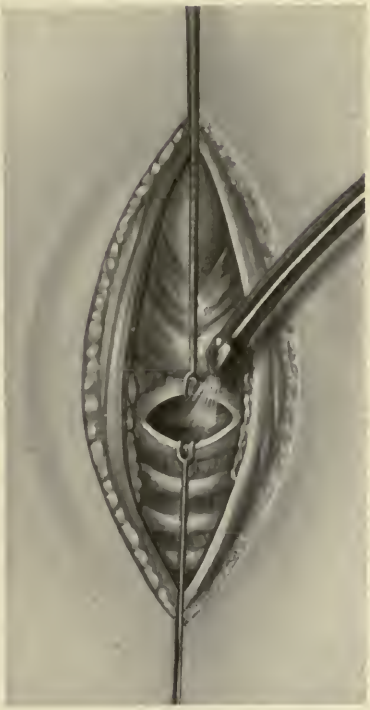


FIG. 67.—LARYNGECTOMY: NOVOCAINIZING THE NERVE-ENDINGS OF THE TRACHEA.

The second stage—the excision of the larynx—is safely and easily accomplished. Each division of skin, subcutaneous tissues, platysma, and mucosa is preceded by a thorough infiltration with novocain. Reflex inhibition of the heart and respiration

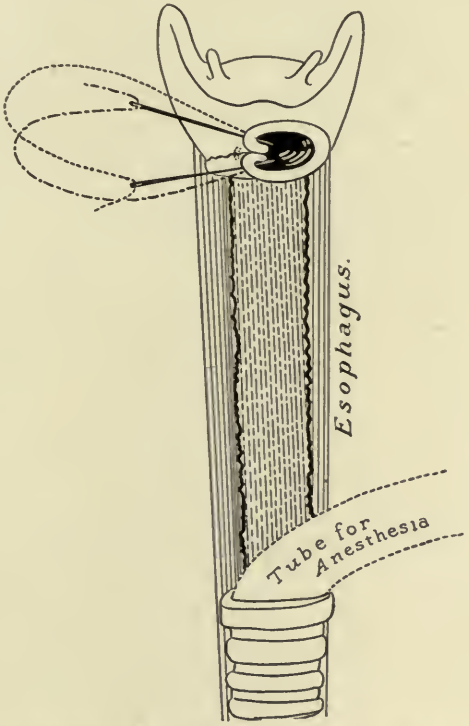


FIG. 68.—LARYNGECTOMY: SCHEMATIC DRAWING SHOWING ARRANGEMENT OF TUBE THROUGH WHICH THE INHALATION ANESTHESIA IS ADMINISTERED AND ALSO THE SHOEMAKER'S STITCH USED IN CLOSING PHARYNGEAL OPENING.

through mechanical stimulation of the superior laryngeal nerves may be absolutely prevented by the hypodermic administration of atropin $\frac{1}{100}$ gr. (adult dose) before the operation, and during the operation by the local use of novocain applied either by a spray or hypodermically. Laryngectomy is usually followed by

a brisk reaction; but since the mediastinum has been protected by the previous gauze packing, and the bronchopulmonary tract has been given a special defense by the preliminary tracheotomy, the patient is well equipped to meet the new condition (Figs. 64–68).

Of 34 laryngectomies, 28 have been performed in two stages, with but a single death.

CANCER OF THE TONGUE

In operation for cancer of the tongue two difficult problems must be met—the immediate surgical risk and the possibility of permanent cure. The principal immediate danger is pneumonia from inhalation of infection from the field of operation, while there is also danger from the exhaustion which is a result of the diminished ingestion of food, the prolonged endurance of the disease, and the operation.

To ensure a permanent cure not only is the cancer to be removed, but the pertinent glands of the neck must be completely excised, whether they be enlarged or not. If both of these operations be performed at the same séance, then the patient may go to the ground because he is unable to bear the burden of the diminished nutrition and the soreness over so large a field as the mouth and neck in addition to the inevitable infection in the mouth. The possibility of a permanent cure depends also on the prevention of the immediate implantation of cancer cells in the mouth at the time of the operation. If the cancer is not large, no cutting operation whatever is made, but with the cautery all the disease in the mouth is destroyed. If, however, the growth be extensive, it is best on one day to cauterize the field of the disease and on the following day, after the cancer cells have died of starvation, to excise the entire cancer field in the mouth. After the patient has well recovered from the mouth operation and is able

to take nourishment satisfactorily, the final operation—excision of the glands of the neck—can be performed without great inconvenience to the patient. Bloodgood has achieved remarkably good results by the cautery method.

In addition to the lessened risk of the extension of the cancer, the two-stage operation lessens also the danger of infection, for when the whole operation is performed at one séance the neck is so sore that the patient is almost certain to inhale infection from the mouth directly, whereas if the neck be normal the patient is able to stand up, to move about, to spit out the accumulations, and thus to protect his lungs against infection.

CHAPTER XIX

ANOCIATION IN RELATION TO THE HANDICAPPED PATIENT

HYPERTENSION

In considering the advisability of operation upon a patient with hypertension, we shall find that while at times the hazard must be taken at once, at times, also, operation may be delayed until the hypertension hazard has been eliminated or to some extent at least diminished. If a patient with a benign tumor be in the throes of an overwhelming grief, or if he be passing through a psychic strain—the result of intense worry or anxiety—the operation may well be delayed until the emotional stress has passed. If the hypertension be due to a pyogenic infection, the operation for a chronic disease may be delayed until the focus has been eradicated. Again, operation for benign tumors or chronic diseases may await the most favorable phase of that form of hypertension which can be partially controlled by nitroglycerin, meat-free diet, rest, and diversion. In these controllable cases, however, we do not meet the great problems, which are: (1) to discover just what are the special risks when operation in hypertension cases cannot be postponed; and (2) to evolve means by which these risks may be minimized or obviated.

The natural sequelæ in hypertension cases are embolism, thrombosis, renal insufficiency, angina, pneumonia, and cardiac failure. Why are these dangers precipitated by operation? We know that some of these results are to be expected when the individual with high blood-pressure is subjected to undue mental or

physical exertion; to sudden shock, either physical or psychic; or to heavy nervous strain. From such cases a heavy toll of life is levied at seasons of great stress. In the hypertension case the avoidance of excitement is desirable, although the patient seems rugged and strong and confident. The surgeon must not allow himself to be misled; he must look upon this man as a bridge upon which has been loaded all the weight it can hold. It is the last pound that causes the crash. Until the crash, all seems well. These patients should be managed just as nearly like a case of exophthalmic goiter as possible. Complete *anociation* is indicated. There must be freedom from excitement, minimum trauma, maximum protection. Ether, especially, is to be avoided. Preliminary rest, preoperative morphin, and sleep on the night before operation are important. These precautions may seem exaggerated, but experienced clinicians will understand their significance.

NEPHRITIS

In the presence of nephritis adequate preparation is essential. Ensure rest; prescribe nephritic diet; urge water; avoid anxiety, dread, worry; and in general follow the plan already outlined for cases of hypertension.

DIABETES

In the surgical treatment of patients with diabetes the prime essential is to defer operation until the urine has been made free from sugar, acetone, and diacetic acid by the Allen starvation treatment. Then operate under complete *anociation*, as in cases of nephritis and of hypertension. It is well to bear in mind that the diabetic bears opium well. Our statistics include 15 amputations for diabetic gangrene; and a study of the postoperative course of these cases shows an enormous difference between the results of operations on carefully prepared diabetic patients and the results of the operations on unprepared cases.

PREGNANCY

When an operation on a pregnant patient is required the more nearly the treatment approximates the treatment of a case of exophthalmic goiter, the less is the probability of a resultant miscarriage.

CHAPTER XX

THE RELATION OF ANOCIATION TO POSTOPERATIVE MORBIDITY

The best clue to the comparative value of different operative methods is found in a study of the postoperative morbidity.

After operations performed under ether anesthesia alone surgeons note a familiar train of sequelæ. Unfortunately, not all of these are absent after operations under *anociation,* but while some are obviated, all are markedly mitigated.

It has already been stated that a study of the pulse during and after the operation perhaps gives us our best clue to the value of the protective technic of *anociation* and explains the strikingly decreased postoperative morbidity after anociated operations. A comparison of 500 consecutive cases operated upon under ether with 500 consecutive cases operated upon under *anociation* showed in the ether cases an average increase of 21.6 beats during the operation, while the anociated cases showed an average fall of 0.83 beat during the operation.

Among the postoperative sequelæ that are greatly diminished are gas-pains after abdominal sections. And one of the most gratifying improvements is the striking diminution of the postoperative nervousness and postoperative neurasthenia. This improvement is analogous to the diminished hyperthyroidism, and the more speedy convalescence after the anociated surgical treatment of exophthalmic goiter. The more nearly the nervous system is maintained in a tranquil state, the less the nervous reaction.

NAUSEA AND VOMITING—DIGESTIVE DISTURBANCES

The intensity of these postoperative symptoms depends upon the field of the operation; on the inhalation anesthetic; on the amount of postoperative pain; and on the gentleness or roughness of the operator. Appetite may be driven away and digestion may be broken down by even a simple operation on any part of the body if it be crudely and roughly performed under ether anesthesia, or if the tension of the stitches be too great and the dressings too tightly applied.

On the other hand, except for the occasional occurrence of morphin nausea, nausea and vomiting may be obviated and the digestive impairment will be minimized by nitrous oxid-oxygen anesthesia, sharp-knife dissection, the gentle manipulation of tissues, cautious despatch in operating, complete nerve blocking during the operation and for several days thereafter, and the careful insertion of stitches and application of bandages. No matter how extensive or what the location of the operation, if it be performed under complete *anociation*, a nursing mother will be able to give each regular feeding, and the babe will give no token of digestive disturbance.

BACKACHE

In anociated operations the patient rests on the operating-table on a warm water-bed. For this reason, and since the muscles are not relaxed under the mild nitrous oxid-oxygen anesthesia, heavy strain on the ligaments and joints is eliminated, and backache is prevented, except that backache which is produced by the technic of certain abdominal operations, such as supravaginal hysterectomy. In our comparative study we found that in the postoperative bedside notes of 500 cases operated upon under ether anesthesia backache is mentioned in 91 cases, while in 500 cases under *anociation* it is mentioned only 30 times.

NEPHRITIS

The lipoid-solvent action of ether is sufficient reason for the ether nephritis, as the renal epithelium contains much lipoid substance. The use of nitrous oxid-oxygen does not cause nephritis.

PNEUMONIA

The diminution of the number of cases of postoperative pneumonia since the adoption of the technic of *anociation* is striking. The more careful handling of tissue, especially in abdominal operations, the avoidance of ether, the absence of vomiting, the ability to sit up promptly, and to move about earlier, the lessened depression of the circulation, the absence of mucus, may reasonably account for this very important improvement.

These results return to the nursing staff, to the professional staff, and to ourselves the reward for the labor and patience, the observation, analysis and errors, and the laboratory experimentation, all of which have contributed to the establishment of the principle of *anociation*.

CHAPTER XXI

THE TRANSFUSION OF BLOOD

THE special points of interest and importance in relation to the transfusion of blood are:

1. The technic of transfusion.
2. The fate of transfused blood.
3. Blood reactions.
4. The physiologic effect of transfusion.
5. The danger of transfusion.

TECHNIC OF TRANSFUSION

Methods.—(*a*) *Direct.*—The safest but the most difficult method of transfusion is by vessel to vessel—artery-to-vein or vein-to-vein—anastomosis. The indirect methods are now preferable.

(*b*) *Indirect.*—There are now excellent indirect methods of transfusion, such as the collection of blood from the donor directly from the vein into paraffined glass receptacles, from which it is introduced into a vein of the recipient. Good models of these receptacles are the Vincent, the French, and the Kimpton-Brown (Fig. 69). The syringe methods of transfusion are also quick and useful—*e. g.*, the Lindeman and the Unger. The simplest of all is the citrate method. Whatever method is employed, the two special dangers to be avoided are: (*a*) clotting, and (*b*) fragmentation of the red corpuscles. Clotting is prevented (*a*) by keeping free from injury the intima of the blood-vessels which is in contact with the blood-stream; (*b*) by washing away all thromboplastin in the tissue wound and the blood-vessel wound with saline

or citrate solution; (*c*) by carefully paraffining the receptacles and tubes employed (Fig. 70).

FIG. 69.—TRANSFUSION TUBE DEVISED WITH THE AID OF THE STAFF OF A CASUALTY CLEARING STATION. (Capacity 450 c.c. Made by Gentite, Paris.)

THE FATE OF TRANSFUSED BLOOD

The matched whole blood of a normal animal transferred to another animal of the same species functions normally.

BLOOD REACTIONS

The transferred blood of normal individuals of the same species may cause reactions—occasionally serious reactions. This can be obviated by proper grouping. If this has not been done, a very small amount of blood only should be given and symptoms

noted. If at the beginning of a transfusion there is precordial pain, restlessness, respiratory distress, urticaria, flushed face, sweating, it would be well to stop the transfusion. If the condi-

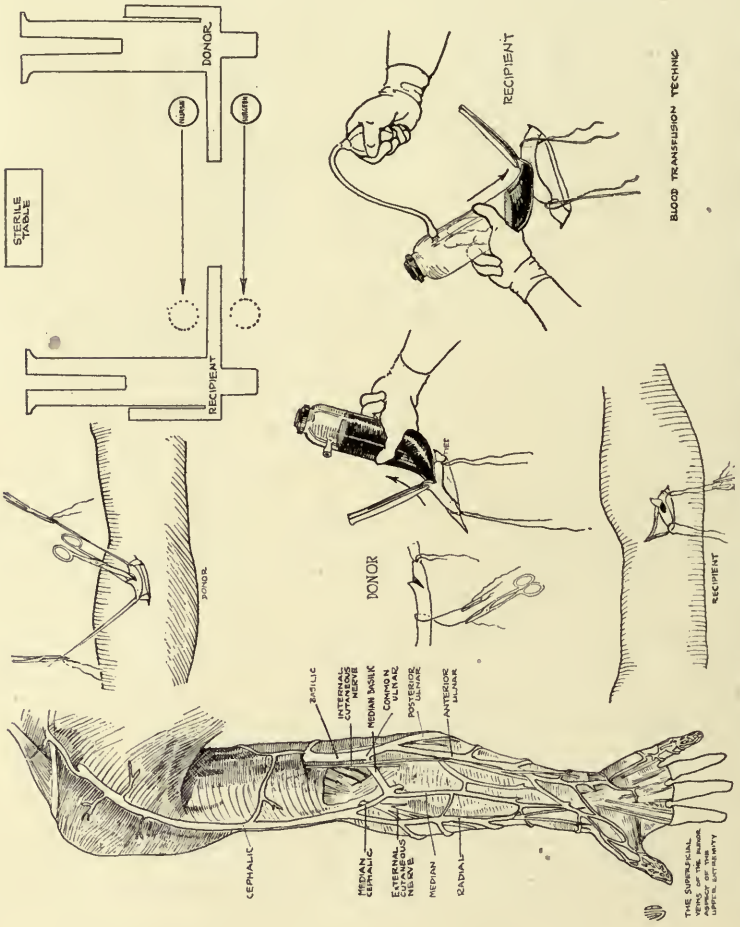


FIG. 70.—TECHNIC OF THE TRANSFUSION OF BLOOD WITH THE TUBE PICTURED IN FIG. 69.

tion is urgent, then, in the face of these symptoms, a large dose of morphin is given and the transfusion is cautiously continued. If time permits, however, the compatibility of the blood of the donor and recipient should always be established by the method

of Brem.[1] This is especially required in patients having infectious or chronic diseases. In some cases prolonged infection apparently causes changes in the blood—changes dangerous for transfusion. Such changes are infrequent in acute hemorrhage or shock in otherwise normal individuals. In military surgery we found greater tendency to blood reactions at the base hospitals, where infections are common, than at the front area, where the patients were freshly wounded but otherwise normal.

Grouping is, therefore, highly important. Short-cut methods have been developed by Moss, Lee, and Karsner,[2] to the last named of whom we are indebted for the following notes:

BLOOD GROUPS

"Any of the standard methods for demonstration of agglutination may be applied, but that recommended by Lee appears to be the simplest and quickest. For this test it is necessary to have the sera in individual Groups 2 and 3 (Fig. 71). A platinum loopful of each of these sera is placed on a clean microscope slide, and to each is added either an equal amount of whole blood, or blood placed in 1 per cent. sodium citrate solution or in physiologic saline solution. In reading the agglutination care must be taken not to confuse rouleaux formation for agglutination. The test is routinely carried out as follows:

"From ½ to 1 c. c. of 85 per cent. sodium chlorid solution is placed in a small test-tube into which are dropped 2 drops of the blood to be tested. If a clot forms, a satisfactory emulsion of cells can be made by shaking the tube. A platinum loopful of each of the standard sera is placed on a clean slide, and into each drop a loopful of the blood emulsion is rubbed. The reading of the agglutination is made under the microscope (16 mm. objective) and is usually complete in from five to fifteen minutes. As will be seen from the table, if both drops show agglutination, the blood is Group 1; if neither shows agglutination, it is Group 4; and if one shows agglutination and the other not, the blood belongs to

[1] Jour. Amer. Med. Assoc., July 15, 1916. [2] Ibid., March 16, 1918

the group in which there is no agglutination. A somewhat smoother emulsion may be made by inverting the slide so as to convert the drops into hanging drops. The inverted slide can be placed on the microscope stage on another slide whose ends are built up with small pieces of fairly thick slide pasted on with balsam. We frequently use a Group 4 serum as a control. The reaction is so sharp that it is easily read, and if a microscope is not available a lens of 10 diameters' magnification will be quite ample in the hands of a trained worker; and the tests should be

BLOOD GROUPS

SERA OF GROUP

CELLS OF GROUP	1	2	3	4
1	−	+	+	+
2	−	−	+	+
3	−	+	−	+
4	−	−	−	−

+ INDICATES AGGLUTINATION AND HEMOLYSIS. IT WILL BE SEEN THAT THIS GROUPING OF LEE IS THE OPPOSITE OF THAT OF OTTENBERG AND OTHERS

FIG. 71.

carried out by a properly trained man. Reports can usually be handed to the surgeon in fifteen minutes.

"A large list of available donors may be grouped in this fashion, so that when a patient needs a transfusion, his blood may be quickly grouped, and a donor selected from the list posted either in the laboratory or the operating theater. Donors should be free from infectious disease, particularly syphilis.

"It can readily be seen that if a donor is used in the same group as the recipient, the cells of neither will be agglutinated or hemo-

lyzed. Lee maintains, however, that if the donor's serum, according to *in vitro* experiments, agglutinated the recipient's cells, such a donor may be safely used because the donor's serum is thus diluted five to twelve times, and in addition, the recipient's cells are 'amply protected by his own serum,' presumably because of the presence of some antiagglutinative substance. Conversely, if the donor's cells are agglutinated by the recipient's plasma, reactions appear which may be so severe as to be fatal, and at least such a transfusion would be of no value because the agglutinated cells are finally hemolyzed.

"If these statements be true, Group 4 donor may be used for any transfusion, as their cells are not agglutinated by the serum of any group. In the same manner Group 1 may receive blood from any donor, as the serum of Group 1 does not agglutinate any cells. While feeling sure that Group 4 may be used as the 'universal donor' with almost complete safety, the writer prefers to use donors in the same group as the recipient when possible because of his observation of one unfavorable case in which a reaction appeared, the test having shown that the donor's serum agglutinated the recipient's cells as demonstrated by the method of Kolmer. . . . If the standard sera are not obtainable, Lee recommends the following method as the minimum procedure for testing:

"A small amount of blood is collected from a patient (1 c.c. from the ear or finger is sufficient) and allowed to clot. The serum is then obtained. One drop of this serum is placed upon a slide and mixed with a drop of a suspension of blood of the donor taken into $1\frac{1}{2}$ per cent. citrate solution. (A few drops of blood are taken into approximately ten times the amount of one and one-half citrate solution and shaken. It is very important that the blood be dropped directly into the citrate, and should not be partially coagulated.) The test will appear in a few moments, and is best examined under the microscope, where, in the event of a positive test, marked agglutination will be evident. The test will also be evident microscopically. In the event of a negative test it is a wise precaution to raise the cover-glass, and after making sure that the serum and cells are well mixed, to examine the preparation again. The only possible source of confusion is the appear-

ance of rouleaux of the red corpuscles indicating a too thick emulsion. If the test is negative, transfusion may be regarded as entirely safe."

"PERCENTAGE DISTRIBUTION OF GROUPS

"The figures with which the writer is familiar are based on a relatively small number of observations. Statistics of this sort naturally increase in accuracy with the number of observations. Being in a position where a large number of soldiers could be examined, the bloods of 1000 individuals were subjected to examination, with the following results:

	Per cent.
Group 1	3.1
Group 2	42.4
Group 3	8.3
Group 4	46.2
	100.0

"Granting that Group 4 is the universal donor, the chances of a member of any group having a suitable donor in case the blood is not tested are as follows:

Group 1	493 in 1000
Group 2	886 in 1000
Group 3	545 in 1000
Group 4	462 in 1000

"If the group percentage in each group is multiplied by the favorable chances of that group expressed as fractions of 1000, and the results added, the total gives the chance of an individual having a successful transfusion if the bloods are untested. This figure is 649 in 1000."

PHYSIOLOGIC EFFECT OF TRANSFUSION

In normal, as in exhausted animals, transfusion causes a rise in the blood-pressure even to double the normal, the increased pressure being wholly or in part sustained for at least two days. At

the high level thus mechanically established the nervous system exerts no control. After overtransfusion the spinal cord may be anesthetized or destroyed, the medulla divided, or the animal beheaded without causing any change in the blood-pressure. This fact suggests the question: Can an animal be killed by traumatic shock in the presence of a high blood-pressure stabilized by overtransfusion? *It can be killed, but the amount of trauma required is greatly in excess of that required to kill a normal animal not so transfused.*

DANGERS OF TRANSFUSION

One danger of transfusion is an acute dilatation of the heart in debilitated patients. Other dangers are serum reaction, hemolysis, and embolism. If there is time, all these are readily avoided. When the blood-pressure has been low for some time as a result of hemorrhage or shock, the myocardium, like other tissues, is impaired and weak. If blood is transfused rapidly, acute dilatation and immediate death may follow. In this connection it is recalled that when the volume of blood in the heart is increased the work of the heart is augmented in geometric ratio—*i. e.*, if the volume of blood in the heart is trebled, the work of the heart is increased nine times. The symptoms of acute dilatation may be most misleading. The pulse becomes more feeble, the respiratory distress increases, and in the urgency of the moment these phenomena may be interpreted as due to a failing circulation from want of blood—failure just as help is coming. If acute cardiac dilatation should be mistaken for a failing circulation, then disaster is quite sure to follow, for the patient's head will be lowered still more, the infusion of blood accelerated, and death from acute dilatation assured. Whereas, if acute dilatation is promptly recognized, then relief is easily secured. The patient is propped upright; pressure is rhythmically exerted with open hands upon the chest, thus emptying the overdistended heart. The patient is

then laid down, and by rhythmic pressure upon the chest the heart is assisted to do its work. Just as soon as a rising pulse is secured it is well to pause, since the renewed and stronger circulation of blood in the coronary artery will rapidly restore the power of the myocardium. As an aid in this crisis—which is rare—an intravenous injection of digitalone is extremely useful.

How can the correct differentiation be made between acute dilatation of the heart and further collapse from anemia? By percussing the right heart. Before transfusion is begun, the margin of the right heart should be outlined by percussion, and in the first period, until the pulse comes up, the position of the right heart should be noted. In this way the status of the heart may be established with certainty. If in doubt, one should pause and, without changing the position of the patient, make rhythmic compression over the heart. Should there be no dilatation, no harm will be done. If dilatation exists, benefit will result.

The behavior of the heart in these conditions has been experimentally studied with the chest open to direct inspection, while the carotid blood-pressure tracings were recorded on a drum.

With these checks and precautions *blood transfusion becomes safe, simple, and useful.*

How does transfusion minimize shock? By overcoming anemia and, perhaps, in other ways not as yet appreciated.

CHAPTER XXII

ANESTHESIA

The choice of anesthetic lies among the lipoid solvents, ether and chloroform; nitrous oxid-oxygen; and spinal, regional or local anesthesia. In making a choice, we must know (*a*) what damage, if any, is caused by the anesthetic *per se;* and (*b*) what protection, if any, is offered by the anesthetic *per se.*

(*a*) *Ether and Chloroform.*—In normal animals and normal men, as has already been stated, inhalation anesthetics—chloroform and ether more markedly than nitrous oxid—cause increased H-ion concentration of the blood—acidosis—during and about one hour after anesthesia. Protracted ether or chloroform anesthesia causes cytologic changes in the cells of the brain, the liver, and the adrenals identical with those resulting from other causes of exhaustion. After from four to six hours of continuous ether anesthesia many animals die at once; and some never regain consciousness, but die within the first twenty-four hours. Nitrous oxid-oxygen does not injure the brain, but measurably protects it against shock; and, moreover, nitrous oxid-oxygen possesses some of the restorative power of sleep (Fig. 72). Ether and chloroform actively contribute to shock and exhaustion. They should, therefore, be given evenly and lightly, as by the excellent Shipway apparatus. Captain Gregory Marshall has shown that patients may apparently do well during ether anesthesia, but do badly afterward (Fig. 73). These disastrous results follow ether in whatever form it is given, whether (*a*) warm ether vapor and oxygen, (*b*) intravenous ether, or (*c*) ordinary open-air drop ether. The ill effects are due to the damaging chemical effect of

ether. It is an anesthetic only by virtue of this effect, hence it is futile to warm ether or to change the type of inhaler in the expectation that that will modify the damaging chemical effect by virtue of which it is an anesthetic.

(*b*) *Nitrous oxid-oxygen anesthesia* is light and gives less muscular relaxation than ether or chloroform. *Special training in its administration is absolutely required,* for it is technically the most difficult of all anesthetics to administer safely, although its administration is facilitated by recent improvements in the apparatus. These disadvantages, however, are far outweighed by its advantages, as compared with ether or chloroform. It is quick in its action; is pleasant to take; recovery is immediate; it produces no nausea; it is protective—strongly protective—against the shock of operation. *Nitrous oxid-oxygen is almost a specific against shock.* It apparently owes this property to its interference with the use of oxygen by the brain cells, as a result of which the cells cannot expend their energy, and in consequence cannot accumulate acid by-products in response to the trauma of operation. In this sense nitrous oxid is an ideal anociating agent. It is as protective as the local blocking of nerves, but for another reason. Nowhere have the results of the use of nitrous oxid-oxygen been more dramatic than in military surgery in the front areas, as is shown by the charts of Captain Marshall (Fig. 74). These charts could be multiplied indefinitely. They typify every-day results. In any series of grave cases in military surgery the use of nitrous oxid-oxygen alone will improve results in abdominal and chest operations about 25 per cent.; in high amputations, about 100 per cent.

For many minor operations nitrous oxid produces a pleasant analgesia in which pain is abolished while consciousness is retained. It can be given under positive pressure when desired, as in chest operations, maintaining the lung flabbily in the chest, against the

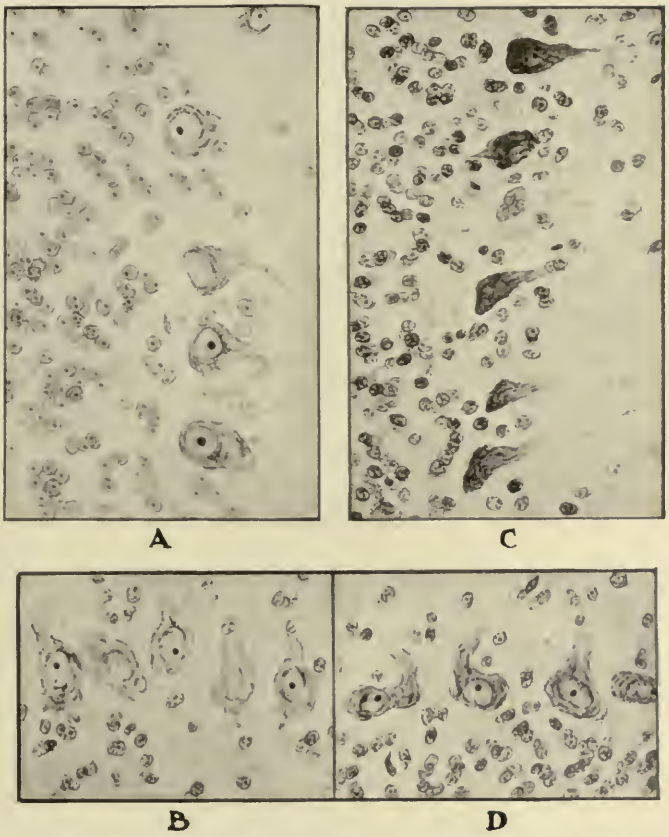


FIG. 72.—RESTORATIVE EFFECT OF NATURAL SLEEP AND OF NITROUS OXID ANESTHESIA ON THE CEREBELLUMS OF RABBITS EXHAUSTED BY PROLONGED INSOMNIA. (From camera lucida drawings.)

A, Section of normal cerebellum of rabbit. B, Section of cerebellum of a rabbit after insomnia one hundred and nine hours. C, Section of cerebellum of a rabbit which during one hundred and nine hours had been under nitrous-oxid anesthesia for one hour out of every six. D, Section of cerebellum of a rabbit which had slept for six hours after insomnia for one hundred and nine hours.

chest wall, or protruding out of the opening in the chest wall, as may be required. It causes neither bronchitis, pneumonia, nor nephritis, and the patients recover so quickly that they can eat and drink soon after the operation. In the case of one patient

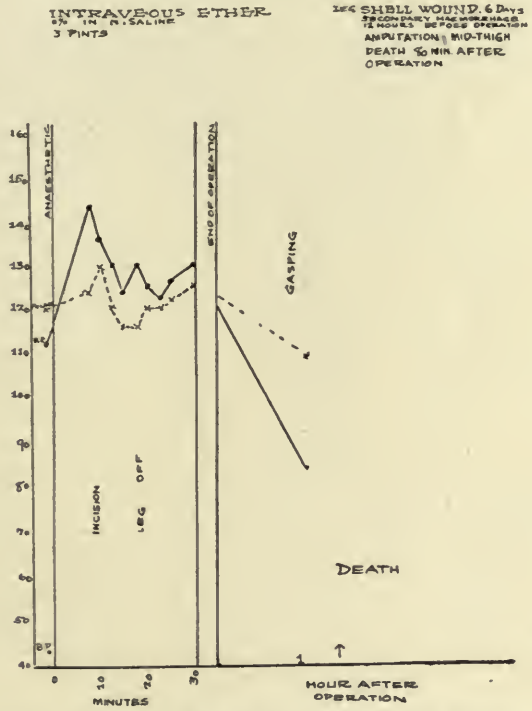


FIG. 73.—CHART ILLUSTRATING THE DISASTROUS *After*-EFFECTS OF ETHER ANESTHESIA. Compare with Fig. 74. (By courtesy of Captain Gregory Marshall.)

Gwathmey has given nitrous oxid-oxygen 139 times, and neither tolerance nor dread was established.

Nitrous oxid, like ether and chloroform, must be pure. The apparatus for its administration must be capable of delivering any desired pressure and mixture of nitrous oxid and oxygen. The induction of anesthesia must be gradual, not too rapid;

and respiration must be established and maintained at an even rate. The patient must be kept pink throughout the anesthesia. *The pink patient cannot die.* If complete anesthesia cannot be secured, as in alcoholics, and the patient kept pink, or if anesthesia is attained, but sufficient relaxation cannot be secured and the

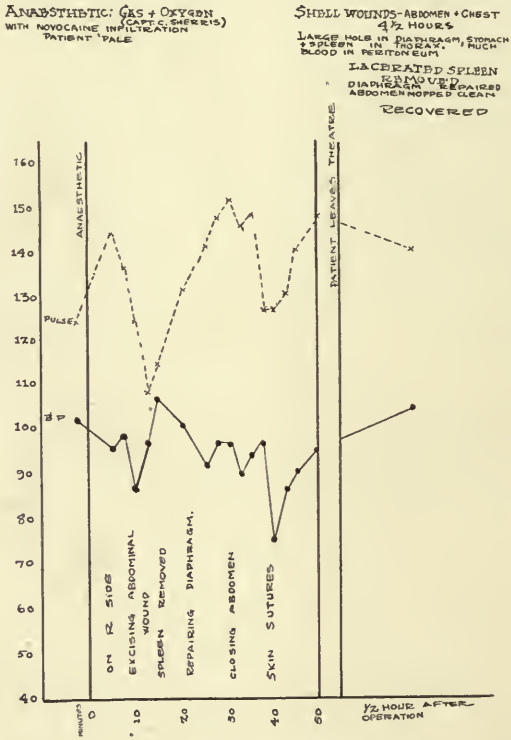


FIG. 74.—CHART ILLUSTRATING THE PROTECTIVE EFFECT OF NITROUS OXID-OXYGEN ANESTHESIA. Compare with Fig. 73. (By courtesy of Captain Gregory Marshall.)

patient kept pink by nitrous oxid-oxygen alone, then sufficient ether must be added. The safety of nitrous oxid-oxygen anesthesia is indicated by the fact that in Lakeside Hospital it has been administered by the chief anesthetist, Miss Hodgins, and by her pupils, over 26,439 times without an anesthetic death.

Because nitrous oxid-oxygen anesthesia is more difficult to give, costs more, and requires more expensive apparatus than ether, this anesthetic seems less satisfactory to the operator; but because its protection is so great, its inhalation so pleasant, its

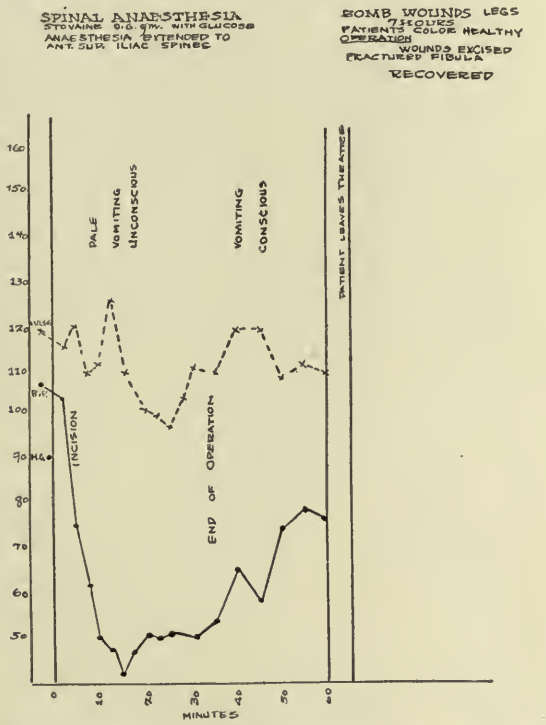


Fig. 75.—Chart Illustrating the Immediate Fall in Blood-pressure Resulting from Spinal Anesthesia. (By courtesy of Captain Gregory Marshall.)

after-effects so slight, it must be regarded as strictly the patient's anesthetic.

(*c*) *Spinal Anesthesia.*—Captain Marshall's observations show that one of the immediate effects of spinal anesthesia is the fall in blood-pressure (Fig. 75). This has been conclusively shown in experiments on animals in our laboratory. Captain Marshall has

shown that the fall in blood-pressure is most severe in the recently injured patient whose blood is dilute, his hemoglobin low. After about forty hours have elapsed since the injury was received, spinal anesthesia is comparatively safe This length of time compares with that required for stabilizing the circulation by the re-establishment of the normal factors of safety. It is the recently injured man in deep shock who stands most in need of the protection of nerve blocking. In both the laboratory and clinic it has been shown that no amount of trauma upon an area physiologically severed from the brain by a local anesthetic, by blocking of the spinal cord, or the nerve trunks, or by local infiltration can cause shock. In this manner, so far at least as trauma is concerned, a shockless operation may be performed, but the sights and sounds of the operating-room; the patient's knowledge that his flesh is being divided by a knife; that his blood-vessels are being divided and tied; the sound of the saw that severs his bones—all these contribute to psychic shock. Spinal anesthesia is, therefore, of value provided that the consequent great fall in blood-pressure may be prevented and that the psychic factor may be eliminated. The technic of Colonel Hugh Cabot is excellent. He injects between the fourth and fifth lumbar vertebræ 2 c.c. of a 5 per cent. solution of novocain with adrenalin diluted with 2 c.c. of spinal fluid. At this level the splanchnic area is not so markedly affected and the blood-pressure falls but slightly.

(*d*) *Local Anesthesia,* when applicable, is excellent. When local anesthesia is used it is best to give morphin or omnopon in advance.

CHAPTER XXIII

SUMMARY

THE development of the principle of *anociation* and its application to the operations described in this monograph are the result of prolonged laboratory experimentation; of critical comparative study of the clinical data of operations performed at the Lakeside Hospital under ether alone, under nitrous oxid-oxygen alone, and under complete *anociation;* of the remarkable opportunities for observation during military field service; and of the practical experience gained by the authors and their associates in the treatment, with and without *anociation,* of over 46,809 surgical cases.

In this monograph we have endeavored to show that many causes—singly or in combination—may cause shock, and that shock may be produced by physical trauma with or without inhalation anesthesia; that in the distribution of the defending nociceptors we have a brief epitome of our phylogenetic struggle for existence, as a result of which the most shock-producing injuries are those which affect those parts of the body which have the greatest number of nociceptors and those which defend the most important regions by muscular action. We have shown that nitrous oxid-oxygen anesthesia as compared with ether anesthesia protects against shock—is a true anociative agent—because of its interference with the use of oxygen by the brain cells. We have shown that physical exhaustion is the result of demonstrable changes in certain organs—notably the brain, the liver, and the adrenals—and that those changes when caused by trauma are due to an adaptive response of certain vital parts of the organism to the injury—a silent, motionless effort to escape from the physical

injury of the operation, and that, therefore, if the field of operation be blocked by local anesthesia, or if the nerve connection between the brain and the injury be blocked, or if the brain cells are prevented from making an adaptive response, the physical injury alone cannot cause shock. We have shown that the motor mechanism may be powerfully driven by psychic stimuli—perhaps as powerfully as by traumatism and physical exhaustion—and that corresponding changes are produced in the organs of the kinetic system. We have seen that when both the traumatic and the psychic stimuli are excluded shock cannot be produced by trauma alone. We have found that the essential pathology of shock is identical, whatever its cause. That is, when the kinetic system is driven at an overwhelming rate of speed—as by severe injury, by emotional excitation, by perforation of the intestines, by the sudden onset of an infectious disease, by an overdose of strychnin, by a Marathon race, by foreign proteins, by anaphylaxis—the result of these overwhelming activations of the kinetic system is a condition which is identical, however it may be clinically designated, whether surgical or traumatic shock, toxic shock, anaphylactic shock, drug shock, exhaustion, etc., or whether in the absence of activation the cells are injured by altered or suspended internal respiration, by starvation, by hemorrhage, by cold, by inhalation anesthetics, etc.

The cytologic changes characteristic of shock and exhaustion, however caused, we believe to be due to intracellular acidosis. Intracellular acidosis interferes with intracellular respiration, *which is life itself*. This conception seems to us to explain the symptoms of shock and to guide us to a means of prevention and treatment. Impaired internal respiration of the cells of the brain would result in impaired mental action, impaired muscular action. Impaired muscular action and impaired brain action results in the production of less heat, *i. e.*, a lowered temperature. Relaxation

of the muscles, with relaxation of the vascular system, results in a lowered blood-pressure. Internal respiration is interfered with by secondary causes, such as anemia. If the intracellular exhaustion is not complete, then the transfusion of blood improves—cures the shock. If intracellular exhaustion is complete, then, despite a full pulse created by the transfusion of blood, the improvement is only apparent, not real.

In the laboratory, in overtransfused animals, we caused death by trauma during a good blood-pressure and good respiratory exchange; hence the fundamental cause of shock lies beyond the circulation. In our laboratory the presence of blood acidosis in shock was first observed. We found also that anesthetics cause acute blood acidosis, but that alkalies do not prevent anesthesia; nor are they of any considerable use in the treatment of shock. The treatment is directed toward securing physiologic rest, maintaining the body temperature, reinforcing the circulation, and lessening the intracellular acidosis. *The best cure of shock is prevention.*

As a corollary to this theory an operative method has been evolved by means of which shock is minimized or eliminated accordingly as the principle of *anociation* is partially or completely applied.

The practical value of *anociation* is attested by the fact that in the authors' clinic both the mortality rate and the postoperative morbidity have been reduced by the application of this principle; and by the fact that when tested on an enormous scale in the vast surgical theater of the war the principles of anociation have been clearly sustained.

Were it possible to add to the surgeon's experience an expression of the subjective symptoms of the patient, the proof of the value of *anociation* would be even more striking. There is no longer any need of the postoperative recovery room; the work of

the nurses is lessened; and the clinical aspect, both in and out of the operating-room, is altered.

The achievement of these results means a thorough understanding of the principles on which the technic is founded. It necessitates the intelligent and special training of assistants, interns, anesthetists, hospital officials, and nurses. It means a careful hand and a sharp scalpel. It presupposes attention to anything that is for the good of the patient. It means that no detail is too petty for the careful attention of the surgeon himself. Above all, it means that from the patient's first appearance in the surgeon's consulting room, throughout the entire cycle of hospital entrance, operation, and exit from the hospital, there must be no rough points of contact, either psychic or physical.

If performed perfunctorily, as a dull ritual, the technic of *anociation* will fail; it can accomplish its purpose only when each detail, however minute, is considered from the viewpoint of the individual patient.

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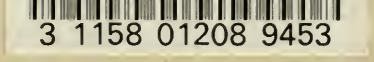
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